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Vol. 40 AUGUST, 1956 No. 2

# SURGERY

*A Monthly Journal Devoted to the Art and Science of Surgery*

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## Original Communications

Prophylactic Treatment of Cancer. Ernesto P. Cruz, M.D., Gerald O. McDonald, M.D., and Warren H. Cole, M.D., Chicago, Ill. ---- 291

Pancreaticosplenectomy Combined With Gastrectomy in Cancer of the Stomach. Komei Nakayama, M.D., Chiba, Japan ---- 297

Pancreatic Function Studies Before and After Thoracolumbar Sympathectomy and Splanchnicectomy for Chronic Relapsing Pancreatitis. Robert B. Pfeffer, M.D., and J. William Hinton, M.D., New York, N. Y. ---- 311

Traumatic Injuries of the Pancreas. Ralph J. Culotta, M.D., John M. Howard, M.D., and George L. Jordan, M.D., Houston, Tex. ---- 320

The Effects of Hypothermia on the Physiology of the Nervous System. Hubert L. Rosomoff, M.D., New York, N. Y. ---- 328

Survival of Cortisone- and Corticotropin-Treated Rats During Exposure to Cold. Andrew Kirsteins, M.D., M.S., Chicago, Ill. ---- 337

Gracilis Muscle Transplant for Rectal Incontinence. Kenneth Pickrell, M.D., Nicholas Georgiade, M.D., Carter Maguire, M.D., and Hugh Crawford, M.D., Durham, N. C. ---- 349

*(Contents continued on inside back cover)*

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Vol. 40, No. 2, August, 1956. Surgery is published monthly by The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Mo. Subscription rates: United States and its Possessions $15.00, Students $7.50; Canada, Latin-America, and Spain $15.50, Students $8.00; Other Countries $16.50, students $9.00. Single copies $2.50 postpaid. Entered as Second-Class matter January 20, 1937, at the Post Office at St. Louis, Missouri, under the Act of March 3, 1879. Printed in the U. S. A.

SURGERY

VOL. 40 AUGUST, 1956 NO. 2

## Original Communications

# PROPHYLACTIC TREATMENT OF CANCER

## THE USE OF CHEMOTHERAPEUTIC AGENTS TO PREVENT TUMOR METASTASIS

ERNESTO P. CRUZ, M.D., GERALD O. MCDONALD, M.D., AND WARREN H. COLE, M.D., CHICAGO, ILL.

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TWO years ago the senior author conceived the idea that, although the chemotherapeutic agents utilized today in the treatment of advanced cancer might not cause any more beneficial effect than improvement in symptoms (perhaps without a significant increase in life span), they might be much more effective from the prophylactic standpoint. Their utilization in a prophylactic way would be dependent upon their use in a very early stage of cancer when the cells do not have a significant vascular "root"; the best example of this stage of cancer would be the dissemination of cancer cells into veins by manipulation of the tumor, and into adjacent tissue by contamination as the tumor is removed. It seems rather obvious that these cancer cells would be much more vulnerable to destruction by chemicals while they are loose and floating and before they acquire a vascular attachment. Herein we are reporting data showing that prophylactic treatment in the animal is effective; as a result we have adopted the plan in the care of patients with cancers of certain types.

*Evidence of Spread by Implantation and Venous Emboli in the Human Patient.*—The important question is how often is cancer spread by dissemination of cells during the operation? The profession has known for decades that there is danger of implantation of cells during operation, and evidence of this has given rise to the extreme caution the surgeon takes not to cut through tumor tissue while performing a radical resection of the breast for cancer. It is surprising, however, that until recently[3, 4, 7, 11] very little attention had been paid to this possibility in carcinoma elsewhere (e.g., colon and rectum). The other pathway of spread during operation is by means of cellular emboli through the veins. Obviously this would not be apt to occur with very great frequency

Supported by a grant from the American Cancer Society (Illinois Division).
Received for publication May 18, 1956.

in tumors which metastasize primarily by lymphatics (e.g., tumor of the oral cavity). However, the majority of the important tumors (e.g., rectum, colon, thyroid, breast, prostate and so forth) metastasize to a great extent by vein. This point surely needs little supporting data; metastases to bones, lungs and liver are examples of this mechanism. For many years pathologists have been calling attention to the growth of cancer into veins within the tumor.[1, 2, 8] We became alarmed at the possibility of spread of cancer by this method, and after demonstration of cancer cells in the fluid perfused through the artery into the veins, advise and now perform ligation of all major vascular trunks leading to and from a tumor (e.g., colon) as soon as the abdomen is opened and before resection is begun.[5] The danger of spread by vein is further emphasized by the very important contribution made by Fisher and Turnbull[6] in which they reported finding cancer cells in the veins of specimens of carcinoma of the colon removed at operation in 32 per cent of 25 specimens examined.

*Effect of Prophylactic Chemotherapy in Animals.*—In an experimental attempt to combat venous spread of tumors of the intestinal tract, it appeared logical to use a tumor which grew well in the animal's liver, because the liver is the important site of metastases from such lesions as colon, rectum, stomach, and so forth. We decided to use the Walker carcinosarcoma 256, because it was a rat tumor which would grow readily in the liver when cells were injected into the portal vein, and would kill rapidly. We made a suspension of cells according to methods described by Breedis and associates[10] and injected a suspension of 110,000 to 150,000 cells into the portal vein of control rats, and rats to be treated. We injected as many control animals as rats to be treated, and made sure that the dose was the same in the two groups of animals. We would like to emphasize that we lost a great number of animals (15 to 30 per cent) from hemorrhage and other causes during the twenty-four-hour period following injection, thus accounting for the different number of animals in the control and the treated groups. We observed the animals and compare the percentage of "takes" in the controls with those in the treated series. We are making no claim for originality in this type of experiment, but as far as we know no one has applied this principle to treatment of human cancer.

We first tried azaserine but in a series of 44 control and 42 treated animals we noted no effect as the percentage of "takes" in the two series was approximately the same, 88.6 and 95.2 per cent, respectively. We then tried nitrogen mustard, first injecting 0.25 mg. of the agent per kilogram of body weight into the portal vein about one minute after the cell suspension was injected. The animals to be treated were injected before the control animals to be sure the animals to be treated would get the more virulent cells in case the added age of the suspension (thirty to sixty minutes) exerted any deleterious effect on virulence of the cells.

In Table I we have listed the results of four different experiments revealing the effect of one injection of 0.5 mg. nitrogen mustard per kilogram of body weight into the portal vein one minute after the injection of the suspension of cancer cells. The same number of cells (110,000 to 150,000) were injected into the control rats as were injected into the treated rats. The percentage of "takes" was 97.4 per cent in 38 control animals and 19.4 per cent in 36 treated animals.

TABLE I. EFFECT OF ONE DOSE (0.5 MG. PER KILOGRAM OF BODY WEIGHT) OF NITROGEN MUSTARD INTO THE PORTAL VEIN OF RATS ONE MINUTE AFTER INJECTION OF THE CANCER CELLS

| GROUP | | NO. RAT | PER CENT "TAKE" |
|---|---|---|---|
| 1 | Treated | 10 | 30.0 |
| | Control | 7 | 100.0 |
| 2 | Treated | 4 | 0.0 |
| | Control | 10 | 100.0 |
| 3 | Treated | 9 | 0.0 |
| | Control | 10 | 100.0 |
| 4 | Treated | 13 | 30.8 |
| | Control | 11 | 90.9 |
| Total | Treated | 36 | 19.4 |
| | Control | 38 | 97.4 |

In Table II we have listed the results of two different experiments revealing the effect of one injection of 0.5 mg. nitrogen mustard per kilogram of body weight into a systemic vein (foot) one hour after injection of the cancer cells into the portal vein. The same number of cells were injected into the control rats as were injected into the treated rats. The percentage of "takes" was 69.2 per cent in 13 control animals and 8.7 per cent in 23 treated animals.

TABLE II. EFFECT OF ONE DOSE (0.5 MG. PER KILOGRAM OF BODY WEIGHT) OF NITROGEN MUSTARD INTO A SYSTEMIC VEIN ONE HOUR AFTER INJECTION OF THE CANCER CELLS INTO THE PORTAL VEIN

| GROUP | | NO. RAT | PER CENT "TAKE" |
|---|---|---|---|
| 1 | Treated | 7 | 0.0 |
| | Control | 4 | 100.0 |
| 2 | Treated | 16 | 12.5 |
| | Control | 9 | 55.5 |
| Total | Treated | 23 | 8.7 |
| | Control | 13 | 69.2 |

In Table III we have listed the results of injection of one dose (0.5 mg. per kilogram of body weight) of nitrogen mustard into the peritoneal cavity one hour after injection of the suspension of cancer cells into the portal vein. The percentage of "takes" was 85.0 per cent in 20 control animals and 23.5 per cent in 17 treated animals.

TABLE III. EFFECT OF ONE DOSE (0.5 MG. PER KILOGRAM OF BODY WEIGHT) OF NITROGEN MUSTARD INJECTION INTRAPERITONEALLY ONE HOUR AFTER INJECTION OF CANCER CELLS INTO THE PORTAL VEIN

| GROUP | NO. RAT | PER CENT "TAKE" |
|---|---|---|
| Treated | 17 | 23.5 |
| Control | 20 | 85.0 |

It is already known that nitrogen mustard is toxic to the liver. Yet in the treatment of advanced cancer, nitrogen mustard has been given into the peritoneal and thoracic cavities of great numbers of patients with advanced cancer without significant toxic effects, although it is realized that in most cases the agent has been injected into cavities containing fluid perhaps half or more of which is removed just before injection of the nitrogen mustard. Before injecting the chemical into the dry peritoneal cavity we injected it into the peritoneal cavity of a series of animals on four consecutive days in different

doses and different concentration. We found that injection of 0.2 mg. to 0.3 mg. per kilogram of body weight in a quantity of saline solution as small as 20 c.c. produced no visible damage to the peritoneal surface of the intestine, although for a period of several hours ascites of variable degree was produced and frequently this fluid became bloody. We also conducted liver function studies utilizing the thymol, the bromsulphthalein and alkaline phosphatase tests. In about half of the animals given the drug on four consecutive days the tests were definitely but slightly positive; the positive readings returned to normal in fifteen to twenty days. Two of eight animals died after injections as listed above. Accordingly, we realized that the margin of safety in nitrogen mustard therapy is not great. Moreover, the hepatotoxic effect should be increased if the drug would be given on the day of operation, because it is known that a definite but slight hepatic insufficiency is produced by the average major operation. Nevertheless, the relative safety reported in the treatment of advanced cancer gave us assurance that the drug might be given with reasonable safety on the day of operation.

Accordingly, it appears that regardless of the method of administration of nitrogen mustard it is moderately effective (in rats) in preventing the "take" of Walker carcinosarcoma cells when injected into the portal vein. As intimated previously we chose this method of production of tumors because it resembled the mechanism of metastases in carcinoma of the digestive tract.

The results of the experiments reported above are only preliminary and leave a lot of questions unanswered. For example, we must know how effective nitrogen mustard will be when treatment is given twenty-four hours, forty-eight hours, and so forth after injection of the cancer cells. Moreover, we must compare the effects of different chemicals. Since the list of chemicals proved effective in animal tumors is increasing almost daily, this problem of chemical specificity alone represents a tremendous task. Moreover, we are by no means sure we can transfer the results of animal experimentation to human therapy. Screening tests with the human cancer would probably be more valuable, although we realize that these results might not be accurate, since we already know that screening tests in animals do not always conform to the actual effect of chemotherapy.

*Prophylactic Chemotherapy in the Treatment of Human Cancer.*—In view of the delay necessary to obtain answers to some of the questions posed above, and the uncertainty that human cancer would respond according to animal experiments, we believe institution of prophylactic therapy in humans is justifiable. Accordingly, on the basis of favorable results with prophylactic chemotherapy in animal (rat) cancer, and with the knowledge that at operation cancer cells can be disseminated by venous emboli and contamination in the open wound, we have started the use of nitrogen mustard in patients having operation for cancer. We have injected it on the day of operation and on three succeeding days except in the occasional patient when toxic effects were noted, or the critical condition of the patient made further injection of nitrogen mustard dangerous. We are using it in all tumors such as breast, colon, rectum, stomach, and so forth which are known to metastasize by vascular channels as well as by lymphatics.

We have already learned that the toxicity of nitrogen mustard is much more significant in the freshly operated patient than in other patients, and logically so, because the patient operated on for a cancer has sustained a rather severe load. A tendency for postoperative bleeding from the wound area has been noted to occur following nitrogen-mustard therapy. Leukopenia is much more common than reported in the treatment of advanced cancer.[9] Moreover, the wound infections seen in leukopenia do not respond to antibiotics. We lost one patient, an elderly, obese woman, aged 79 years, who had a radical mastectomy for a massive carcinoma and had nitrogen mustard on four successive days beginning the day of operation; she might have died anyway, but in retrospect we believe she should have had no more than one or two doses at the most. We have used the conventional dose of 0.1 mg. per kilogram of body weight, but have decided upon 6.5 mg. as the maximum dose, regardless of weight, because the patient we lost was obese and most of our serious leukopenias have been in obese patients. We have used nitrogen mustard in only one patient having an operation for carcinoma of the rectum as we fear uncontrolled infection because of the large contaminated raw space left in the pelvis.

In this patient we gave one dose intraperitoneally on the day of operation and a second dose intravenously the next day. The course of two additional doses by vein was completed five days later. In patients having abdominal operations for cancer (e.g., colon) we give the first dose intraperitoneally at the end of the operations in 500 to 750 c.c. of physiologic saline solution, and the remaining three doses intravenously on succeeding days as directed. Perhaps our fears are exaggerated because the patient having the Miles operation had a very uneventful convalesence.

Up to date we have given nitrogen mustard to about 20 patients, giving the first dose on the day of operation and the remaining three on the next three postoperative days except in very poor-risk patients. However, we have adopted 70 as the maximum age for this treatment, although patients older than this might safely be given one or two doses.

If our animal experiments are significant, it might be advisable to give the first dose in patients having an abdominal operation for cancer into the portal vein. If this were done, however, we would not have exposed stray cells in the peritoneal cavity to the chemical.

Moreover, it is barely possible that all implants on the peritoneum (a few days to a few weeks old) so small that they are not visible with the naked eye, would be killed with the proper agent. It would be more desirable to give one agent into the portal vein, and another into the peritoneal cavity on the day of operation. If only one agent were used, the dose would have to be split. It would be more desirable to use two chemicals which were not complementary in toxicity. We are working on this problem now. Radioactive gold could no doubt be used in conjunction with nitrogen mustard without significant complementary toxic action.

Since it appears that results of screening the tumor cell against various agents would be desirable, even though we have no definite proof these tests would be valid, we believe this procedure would be justifiable. At least, it

would be better than a plain guess as to which of the dozens of hundreds of available agents should be used. In any event we are adopting the principle of screening the human cells, and are going to give the chemical to which the cells are most sensitive.

## SUMMARY

It is our impression that, at operation, cancer cells may be disseminated as venous emboli, by implantation in suture lines, and by spread of loose cells throughout the wound. Certain precautions will minimize this spread, but we should obviously utilize every possible mechanism in decreasing this possibility.

In some experiments injecting a suspension of Walker carcinosarcoma cells into the portal vein of rats, we have noted that nitrogen mustard given by either of three mechanisms ([1] into the portal vein, [2] into a systemic vein, or [3] intraperitoneally) on the day of injection of the cancer cells will decrease sharply the percentage of "takes." On the basis of these experiments, and with the assumption that "floating" cancer cells are more readily killed than cells with a vascular "root," we have started giving a course of nitrogen mustard, beginning on the day of operation, to patients having tumors which metastasize by vein as well as by lymphatics. Except in poor-risk patients we give a dose each day for four doses. In celiotomies we have given the first dose intraperitoneally, and the remaining three by systemic vein. We have used the conventional dose of 0.1 mg. per kilogram of body weight, except that we are limiting the daily dose to 6.5 mg., and do not give the full course to patients over 69 or 70 years of age.

We are continuing the animal experiments hoping to determine the relative effect when the nitrogen mustard is started at varying intervals after injection of the cancer cells, and utilizing different chemicals. Since so many chemicals are now available having an anticancer effect, we believe screening tests with tissue culture methods would be desirable to obtain the most effective drug for a given tumor, as removed from the patient. We are instituting this screening test method.

## REFERENCES

1. Barringer, P. L., Dockerty, M. B., Waugh, J. M., and Bargen, J. A.: Carcinoma of the Large Intestine: A New Approach to the Study of Venous Spread, Surg., Gynec. & Obst. **98**: 62, 1954.
2. Brown, C. E., and Warren, S.: Visceral Metastasis from Rectal Carcinoma, Surg., Gynec. & Obst. **66**: 611, 1938.
3. Cole, W. H.: Measures to Combat the Menace of Cancer, Am. Surgeon **17**: 660, 1951.
4. Cole, W. H.: Recurrence in Carcinoma of the Colon and Proximal Rectum Following Resection for Carcinoma, Arch. Surg. **65**: 264, 1952.
5. Cole, W. H., Packard, D., and Southwick, H. W.: Carcinoma of the Colon with Special Reference to Prevention of Recurrence, J. A. M. A. **155**: 1549-1553, 1954.
6. Fisher, D. R., and Turnbull, R. B., Jr.: The Cytologic Demonstration and Significance of Tumor Cells in the Mesenteric Venous Blood in Patients with Colorectal Carcinoma, Surg., Gynec. & Obst. **100**: 102, 1955.
7. Goligher, J. C., Dukes, C. E., and Bussey, H. J. R.: Local Recurrences After Sphincter-Saving Excisions for Carcinoma of the Rectum and Rectosigmoid, Brit. J. Surg. **39**: 199, 1951.
8. Grinnell, R. S.: The Spread of Carcinoma of the Colon and Rectum, Cancer **3**: 641, 1950.
9. Hatch, H. B., Bradford, J. K., and Ochsner, Alton: Nitrogen Mustard in the Treatment of Advanced Carcinoma of the Lung, J. A. M. A. **160**: 1129, 1956.
10. Lucke, B., Breedis, C., Woo, Z. P., Beswick, L., and Nowell, P.: Differential Growth of Metastatic Tumor in Liver and Lung: Experiments with Rabbit $V_2$ Carcinoma, Cancer Res. **12**: 734, 1952.
11. Morgan, C. N., and Lloyd-Davies, O. V.: Discussion on Conserative Resection in Carcinoma of the Rectum, Proc. Roy. Soc. Med. **43**: 701, 1950.

# PANCREATICOSPLENECTOMY COMBINED WITH GASTRECTOMY IN CANCER OF THE STOMACH

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## INTRODUCTION

TWO of the current therapeutic concepts in surgery for gastric cancer, total gastrectomy and cardiectomy, have been converted to operative procedures which can be performed with a fair degree of ease and which are followed by low mortality and morbidity. Excluding cardiac cancer, in those patients with gastric cancer in which removal of the entire stomach is necessary, cancerous invasion associated with adhesion of the posterior surface of the stomach to the tail of the pancreas, or metastases into the parapancreatic and splenic hilar nodes are common occurrences. In this situation both the spleen and the tail of the pancreas should be resected en masse, in combination with gastrectomy, thus enlarging the limits of operability.

In the literature from Europe and America, Sweet, Finsterer, Wangensteen, and their associates have advocated the necessity of the combined resection of these adjacent organs with gastrectomy for a radical cure in cancer of the stomach. Extensive surgery for advanced cancer can only be justified by the results achieved. Throughout this paper attention shall be focused upon a procedure which consists of a total or partial gastrectomy with en masse resection of the body of the pancreas and spleen, the pancreas being transected at the neck, leaving only the head of the gland in normal position. The primary purpose of this report is to offer an evaluation as to whether this procedure is deserving of recommendation as a worth-while radical treatment with little postoperative morbidity. Another important function of this paper is to describe the operative method which has been performed quite routinely in the author's clinic with utmost ease and safety. The criticism presented herein is based upon as many as 113 clinical cases and upon a large series of animal experiments using about 100 dogs which have been systematically studied in our clinic.

## IMPORTANT CONSIDERATIONS SUPPORTING THE NECESSITY OF THIS OPERATIVE PROCEDURE

*Direct Infiltration Into the Adjacent Organs.*—Direct infiltration into the adjacent organs in cancer of the cardia or the stomach is as shown in Table I. It will be noted that cancerous invasion of the pancreas is a common occurrence, especially in carcinoma of the cardia or the body of the stomach. A study was

Received for publication Aug. 24, 1955.

*Professor of Surgery.

made for a better understanding of the mode of malignant infiltration toward or into the pancreas. This infiltration may be divided into three grades: (1) that reaching only the capsule of the pancreas, not invading the parenchyma itself; (2) that invading only some part of the pancreatic parenchyma; and (3) that pronouncedly involving the parenchyma. A histologic study of the specimens obtained from 45 patients undergoing pancreatospleno-total gastrectomy revealed that an infiltration of the first grade was seen in 60 per cent, one of the second grade was seen in 35.5 per cent, and one of the third grade was seen in 4.5 per cent. Under these circumstances resection of both organs, the pancreas and the spleen, must, of necessity, be carried out, because it is quite obvious that partial resection or mobilization of these adherent parts serves poorly as a radical cure of these advanced lesions.

*Nodal Involvement.*—After injecting pontamine sky blue into the various zones of the stomach, the lymph drainage from this organ was explored closely during operation. As mentioned repeatedly, metastases from cancer of the cardia or the body of the stomach quite often reach the parapancreatic and splenic hilar nodes, beyond the regional nodes. This incident was well corroborated by our histologic study covering those specimens obtained from 40 patients who were treated by pancreatospleno-total gastrectomy (Fig. 1). This histologic study revealed that the chance of metastases to the parapancreatic and splenic hilar nodes approximated that of invasion of the regional lymph nodes. It will be readily understood that a radical cure for such cancer of the cardia or the body of the stomach is only attainable by the en masse resection of the pancreas and the spleen which, when combined with the removal of the stomach, allows automatic removal of these involved lymph nodes.

TABLE I. SURVEY ON CANCEROUS INFILTRATION TO THE ADJACENT ORGANS (367 CASES)

| | CANCER OF THE CARDIA 78 CASES (PER CENT) | CANCER OF THE BODY OF THE STOMACH 58 CASES (PER CENT) | CANCER OF THE PYLORUS 211 CASES (PER CENT) | CANCER OF THE ENTIRE STOMACH 20 CASES (PER CENT) |
|---|---|---|---|---|
| Pancreas Tail | 62.8 | 46.6 | 0.0 | 30 |
| Pancreas Head | 0.0 | 0.0 | 28.4 | |
| Liver | 15.3 | 13.0 | 5.2 | 5 |
| Retroperitoneum | 12.8 | 0.0 | 0.0 | 0 |
| Diaphragm | 11.5 | 0.0 | 0.0 | 0 |
| Mesocolon | 3.8 | 13.7 | 10.4 | 5 |
| Spleen | 1.21 | 0.0 | 0.0 | 0 |
| Gall bladder | 1.2 | 1.7 | 0.4 | 0 |
| Transverse colon | 1.2 | 8.6 | 8.5 | 10 |
| Ventral peritoneum | 0.0 | 0.0 | 0.9 | 0 |
| None | 16.6 | 41.37 | 56.8 | 60 |

### A RATIONAL SCOPE OF RESECTION OF THE PANCREAS AND THE SPLEEN

One of our purposes was the establishment of a rational scope of removal of these two adjacent organs which would offer maximum success in removal of the malignant tissues with a minimum postoperative ill effect.

The rational transecting line of the pancreas used by us is that line, vertical to the longitudinal axis of the pancreas, which originates at the point

where the middle colic artery and the lower margin of the pancreas meet (Fig. 2). The malignant infiltrative adhesion to the pancreas was found, on the average, to be situated within the portion 6 cm. from the left end of the gland, while this transecting line is located 12 cm. from the same end. This adherent infiltration is completely included in the scope of this resection. The

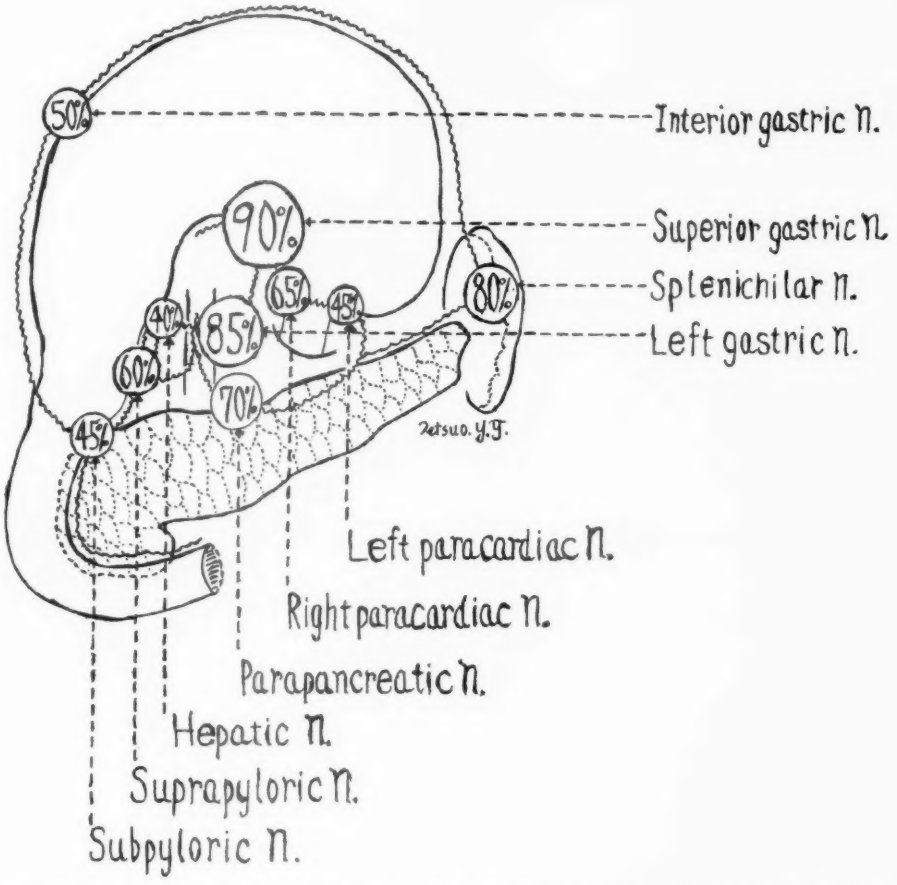


Fig. 1.—Survey on nodal involvement (40 cases with pancreatospleno-total gastrectomy: cancer of the cardia, 22 cases; cancer of the body of the stomach, 18 cases).

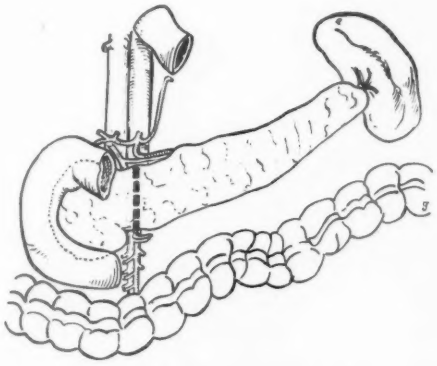

Fig. 2.—Rational transecting line of the pancreas.

rational transecting line is situated slightly to the right of the axis of the celiac artery. If the pancreas is transected along this line, these anatomic relationships allow us not only the automatic removal of the parapancreatic and splenic hilar nodes, but also a better visualization of the hepatic, celiac, and other important nodes involved, thus permitting removal of the latter nodes with ease. This rational transection usually yields resection of one-half to two-fifths of the length of the pancreas, two-fifths to three-fifths of its weight.

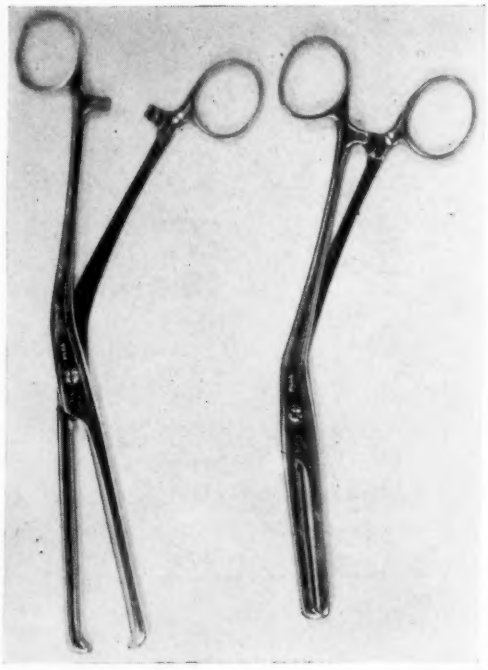

Fig. 3.—Pancreatic crushing clamp.

## OPERATIVE PROCEDURE

*Order of the Operative Procedure.*—The basic study described above indicates that the surgical attack should be placed first in the right retroperitoneal area, rather than in the splenic or the left retroperitoneal space.

*Treatment of the Pancreatic Stump Left in the Abdominal Cavity.—*

*Method:* Before transecting the pancreas, the posterior surface of this organ is mobilized along the proposed transecting line by blunt dissection, and then the pancreas is clamped with two pancreatic crushing clamps juxtaposed to each other along this line, and crushed. When crushed with these clamps, devised by myself, only the parenchyma, vessels, and ducts of the gland are crushed, leaving the capsule intact (Fig. 3). For treatment of the crushed stump, a simple silk ligature placed on the stump is always sufficient. This is a distinguishing feature of our operative method. In other words, neither cauterization nor multiple ligatures are needed, thus securing a minimum chance of bleeding or leakage of pancreatic juices from the remnant stump.

*Animal experimentation on the stump of the remnant pancreas (dogs):* Ten dogs were treated by this simple ligature near the stump of the pancreas. Histologic study was performed upon 3 dogs at one week, 3 dogs at three to five weeks, and 4 dogs at fifteen weeks after operation. From this study we noted that: (1) at one week partial atrophy of the parenchyma near the stump occurred in combination with a marked round cell infiltration as well as production of connective tissue; (2) at three to five weeks the trend toward atrophy of the parenchyma began to subside, and a marked production of connective tissue occurred; (3) at fifteen weeks, the stump was completely replaced by cicatric tissue (Table II).

TABLE II. HISTOLOGIC FINDINGS AT THE STUMP OF THE REMNANT PANCREAS LIGATED WITH SIMPLE SUTURE IN DOGS

| | ATROPHY OF PARENCHYMA | ROUND CELL INFILTRATION | HYPERPLASIA OF CONNECTIVE TISSUE |
|---|---|---|---|
| Postoperative date | | | |
| One week | ++ | ++ | + |
| Three to five weeks | + | + | ++ |
| Fifteen weeks | - | - | +++ |

*Clinical findings:* No postoperative complications due to blow out of the stump were ever experienced. Histologic study on the pancreatic stump, obtained from a patient who died of recurrence three months after operation, revealed a complete healing of the stump, which findings were entirely concordant with the animal experiment.

*Drainage in the Left Lateral Abdomen.*—After removal of these organs, effusions accumulate in the dead space in the left abdominal cavity and interfere with the local healing process. Therefore, a polyethylene film is introduced in this space. The safety of this method of treating the stump was also verified by the fact that no effusions containing pancreatic enzymes were found in any of the cases.

## FUNCTIONAL AND MORPHOLOGIC CHANGES IN THE REMNANT PANCREAS

*Exogenic Secretion.—*

*Experimental study with dogs:* Exogenic secretion obtained from the external pancreatic fistula was investigated with 6 normal dogs, 32 dogs with partial pancreatectomy (8 dogs were used for each of the following resections: one-fourth, two-fifths, three-fifths, and four-fifths), 14 dogs with pancreatosplenototal gastrectomy, 4 dogs with pancreatosplenocardiectomy, and 2 dogs with pancreatosplenectomy. The emphasis of the investigation was placed on those dogs which were treated with two-fifths or three-fifths pancreatectomy, because these grades of resection of the pancreas were similar to those in the clinical cases. The amount of pancreatic juices and the output of enzymes per cubic centimeter were measured by means of insulin, 0.5 per cent hydrochloride, pilocarpine, and milk administration tests. Judged from these data, the following things were noted: (1) The amount of secretion is reduced, in proportion to the extent of pancreatectomy, immediately after operation, and

increases gradually. However, it does not reach the preoperative level at the one-month postoperative date. (2) On the other hand, enzyme activity per cubic centimeter is reduced for one or two weeks after operation, and then increases gradually, often surpassing the preoperative level at three or four weeks. (3) On the contrary, sodium bicarbonate contained in the pancreatic juices is likely to decrease. Briefly, this trend toward concentration of the enzyme occurs in order to compensate for the reduction in the volume of pancreatic juices. When four-fifths of the whole pancreas is removed, however, abnormality occurs in both the volume of secretion and the activity of the enzyme per cubic centimeter, and lasts for a long time. This is obviously a functional decompensation. But, as long as removal of this gland remains less than two-fifths or three-fifths of the whole, no functional abnormality occurs (Fig. 4).

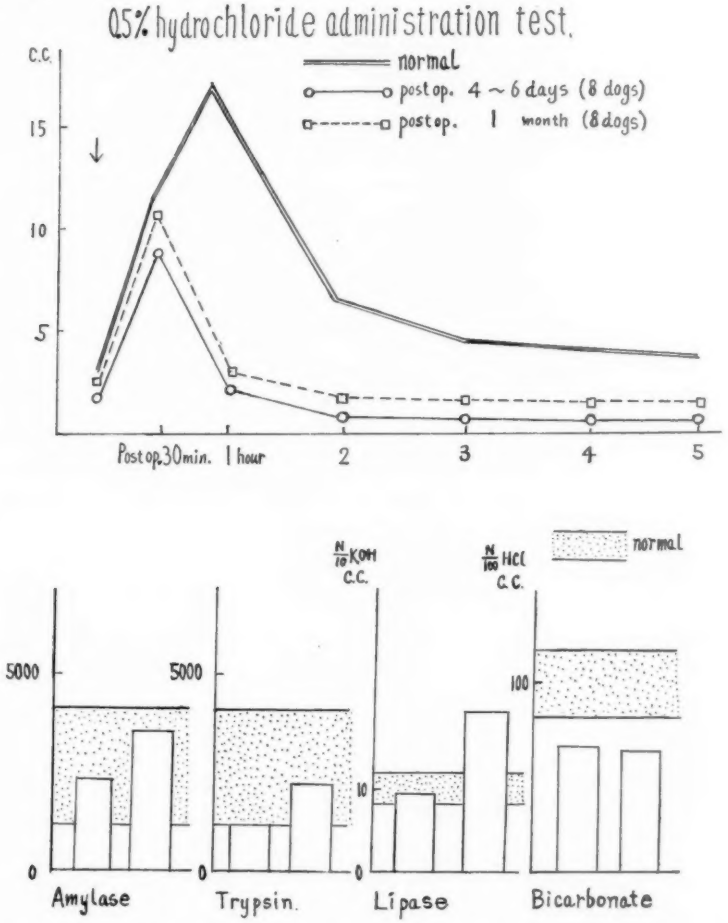


Fig. 4.—Amount of pancreatic juices. Study of exogenic secretion of three-fifths pancreatectomized dogs.

*Clinical information:* By means of a duodenal tube connected with a suction pump, the duodenal juices were taken out under 50 mm. mercury column. The duodenal juices obtained in this way confirmed the animal experiment

with a similar result, and a smooth recovery was effected with the elapse of time. No appreciable difference was found between gastrectomy and this operative procedure (Fig. 5).

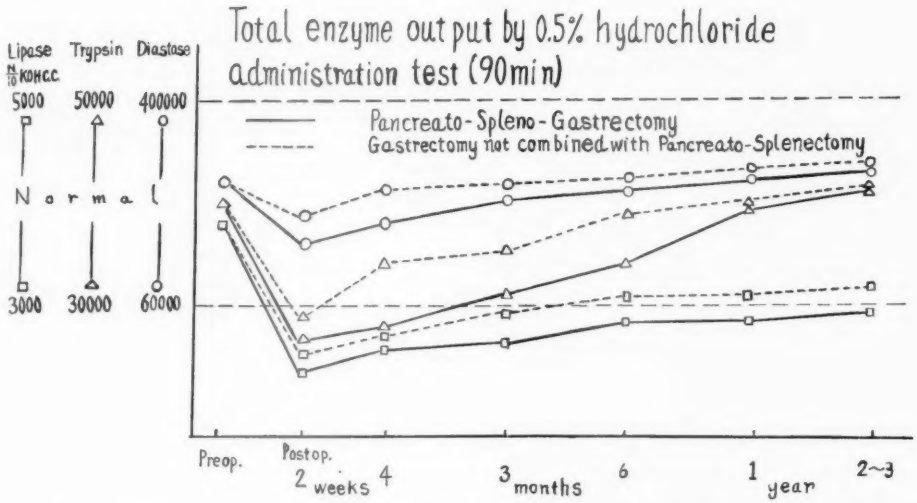


Fig. 5.—Enzyme output (volume by activity). Study of exogenic secretion of three-fifths pancreatectomized dogs.

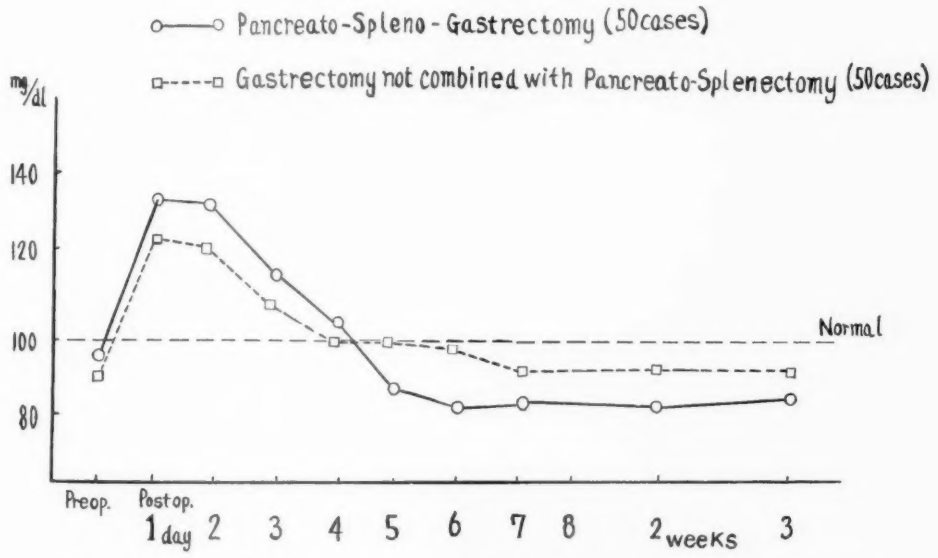


Fig. 6.—Fasting blood sugar level. Study of endogenic secretion in men.

*Endogenic Secretion.—*

*Experimental study with dogs:* Endogenic secretion was also investigated using those animals which were used for study of exogenic secretion. This study covered determination of the fasting blood sugar level, serum amylase concentration, and vagostigmin administration test, intravenous glucose administration test, duplicate glucose administration test via gastrostomy, and others. In the dogs treated by less than two-fifths or three-fifths pancreatec-

tomy, no marked changes were found in fasting blood sugar level and serum amylase concentration, but tests for sugar assimilation revealed abnormalities which lasted about three or four weeks, none of which were signs of diabetes mellitus.

*Clinical studies:* These studies, which were similar to those in the animal experiments, were performed upon the patients treated by this operative method. Although there appeared an ill effect on sugar assimilation, it subsided within six months to one year. No remarkable differences were elicited between gastrectomy and pancreatosplenogastrectomy (Fig. 6).

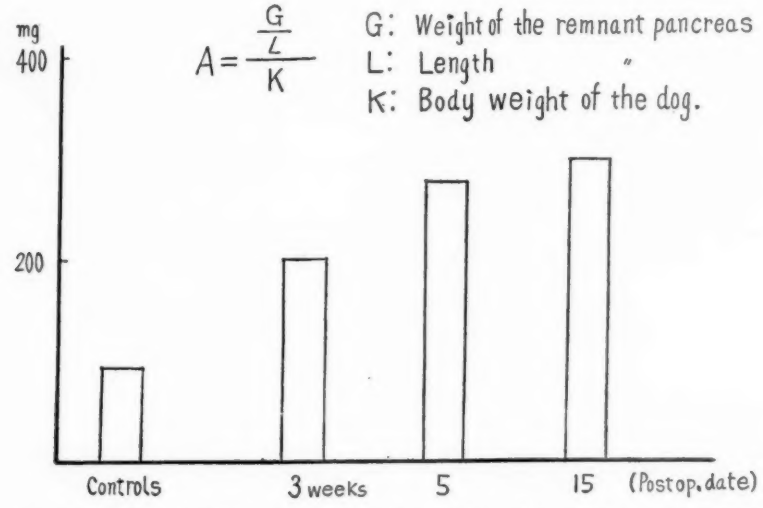


Fig. 7.—Increase in weight of the remnant pancreas in three-fifths pancreatectomized dogs (average of 8 dogs).

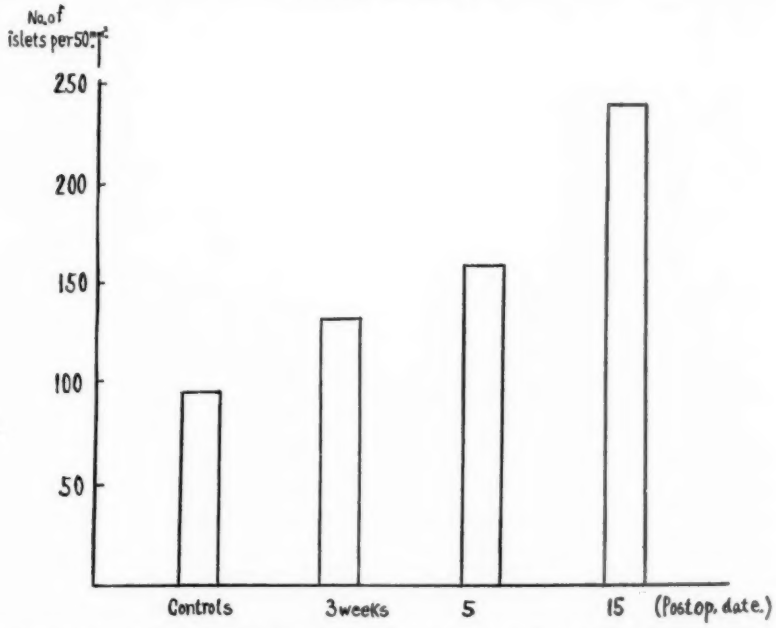


Fig. 8.—Increase in number of Langerhans islets in three-fifths pancreatectomized dogs (average of 8 dogs).

There were two patients who had an episode of hyperglycosuria before leaving the hospital. Both of them had a history of diabetes mellitus. They were treated by insulin and cured by the twentieth postoperative day.

*Morphologic Changes.*—The remnant pancreas was studied for both weight and histologic changes.

*Changes in weight:* The larger the segment of the pancreas resected, the more the remnant portion increases in weight. For example, in the four-fifths pancreatectomized dog, a rapid increase in weight of the remnant portion occurs. It doubles in five weeks and triples in fifteen weeks (Fig. 7).

*Histologic study:* Hypertrophy and proliferation of parenchymatous cells in the remnant gland were found. Specimens were taken from six portions of the remnant pancreas, such as the omental, duodenal, Winslow's, and others, and a comparison between pre- and postoperative periods was made on the islets of Langerhans. In the elapse of as short a time as five to fifteen weeks, the islets of Langerhans showed a marked increase in number in proportion to the extent of pancreatectomy. In the three-fifths or four-fifths pancreatectomized dogs, the islets of Langerhans showed not only an astonishing proliferation, but also a marked hypertrophy into a somewhat different shape. This increase in the number of islets of Langerhans is due to new growth of the islets of Langerhans which originates in centroaciniform cells and in the walls of capillary ducts (Fig. 8). Above all, a marked change appeared in the beta cells, where the beta granules were markedly reduced in number. However, neither hydropic nor degenerative changes, peculiar to diabetes mellitus, were noted (Table III). The functional changes following pancreatectomy, described herein, indicate that compensatory changes, and regenerative signs appearing after about two-fifths removal of the pancreas will remain as physiologic changes.

TABLE III. ALPHA TO BETA CELL NUMBER RATIO IN LANGERHANS ISLETS

| | NORMAL CASES ALPHA:BETA | PANCREATECTOMIZED CASES ALPHA:BETA |
|---|---|---|
| Dogs | 1:2.8 to 3.6 | 2/5 resected cases (2) 1:2.8<br>3/5 to 4/5 resected cases (4) 1:3.1<br>(15-week postoperative date) 1:5.2 |
| Man | 1:3 to 8 | (8-week postoperative date) |

## MAIN VITAL INFLUENCES

Vital influences of this surgical intervention on each important organ and system were studied minutely.

*Liver Functions.*—A comparison between gastrectomy and pancreatosplenogastrectomy was made on the basis of various liver function tests. Eighty patients and 20 dogs were submitted to this study. It is concluded from this study that disturbances of liver function occurring postoperatively improve steadily and disappear eventually. No appreciable aggravation in

liver function was noted throughout the period of follow-up studies. Cholesterol ester remained within or near normal limitations. These data serve in corroborating its few ill effects.

*Vital Reaction Due to Splenectomy Per Se.*—Combined resection of the spleen is the prerequisite for a radical cure in the relatively advanced cancer of the cardia or the body of the stomach. Therefore, to evaluate this operative procedure intelligently it is also quite important to have some understanding of the vital reaction due to splenectomy itself in this situation. The following tests were carried out: blood picture, the amount of flowing blood, iron metabolism, some problems on immunity from malignancy, and vital exploration into vital protective abilities; leukocyte phagocytosis; serum bactericidal; Congo red or communin administration. Although the two former tests showed normal reaction, the two latter ones revealed a reduction in vital resistance lasting about four weeks, especially in splenectomized cases. It is certain that these phenomena, although only temporary, must be attributed to removal of the spleen. Therefore, special care should be paid to the postoperative treatment.

## DIAGNOSIS AND INDICATIONS FOR SURGERY

*Roentgenologic Study.*—Competent x-ray study is essential to determine indications which call for this operative method. Our conclusion, obtained from x-ray study combined with pathology in 110 patients, is: if carcinoma originating in the cardiac portion or the body of the stomach, has infiltrated more than 5 cm. along the lesser curvature of the stomach, there would be a relative indication for this surgical procedure; and if it has infiltrated more than 7 cm. along the lesser curvature, there would be an absolute indication for surgery. This criterion is based upon the fact that infiltration extending more than 5 cm. along the lesser curvature was seen in combination with 70 or 80 per cent incidence of involvement of the parapancreatic and splenic hilar nodes, and that the more than 7 cm. invasion occurred with 100 per cent incidence of nodal involvement.

Another means of evaluating the grade of retroperitoneal infiltration is transparietal splenovenography, now being used on 120 patients with cancer of the stomach. Stenosis, abnormal flexion of the vein, retrograde flow or stagnation of the venous blood, pressure on the vein by the adjacent structures, and irregularity of the venous wall are all suggestive of carcinomatous invasion toward the retroperitoneal space. Intelligent interpretation of these findings adds other important criteria for determining indications for this operative procedure. Marked abnormalities are often indicative of unfeasibility of radical operation (Figs. 9 and 10).

*Diagnostic Method With Radioactive Isotopes.*—About four hours after hypodermic administration of 300 or 500 $\mu c$ of $P^{32}$, laparotomy is performed and the measurement of count is carried out for each group of lymph nodes with the very tiny Geiger-Müller counter. If the test reveals a count of 1.2 or more times normal, these nodes should be removed as far as possible, because, in the majority of them, cancerous involvement is also found by histo-

logic study. This diagnostic method is also helpful in determining whether cardiectomy or total gastrectomy is the procedure of choice in cancer of the cardia.

Fig. 9.

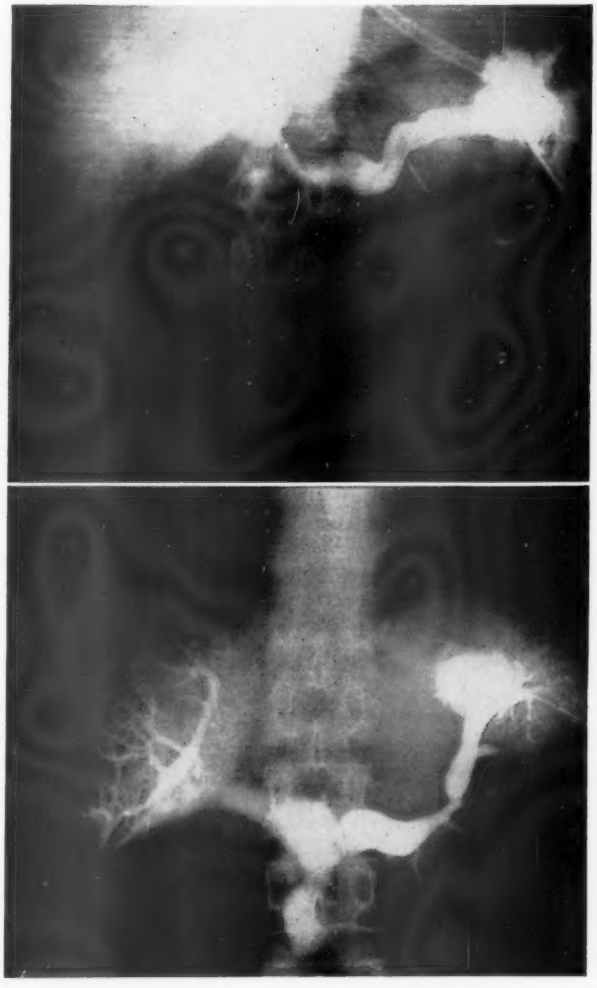

Fig. 10.

Fig. 9.—Pathologic splenovenogram with pancreatosplenogastrectomy still feasible.
Fig. 10.—Pathologic splenovenogram with pancreatosplenogastrectomy no longer feasible.

## STATISTICAL SURVEYS

*Statistical Surveys and Operative Results.*—One hundred thirteen patients with cancer of the cardia or the body of the stomach were treated by pancreatosplenogastrectomy during a period from April, 1950, to March, 1955, in the Nakayama Surgical Department. Operative details are as shown in Table IV. The number of deaths within one month after operation were two during this period, a 1.17 per cent operative mortality (Table V). This operative mortality was less than that of gastrectomy per se, which is 2.94 per cent. Of the two dead patients, one patient expired on the twenty-sixth postopera-

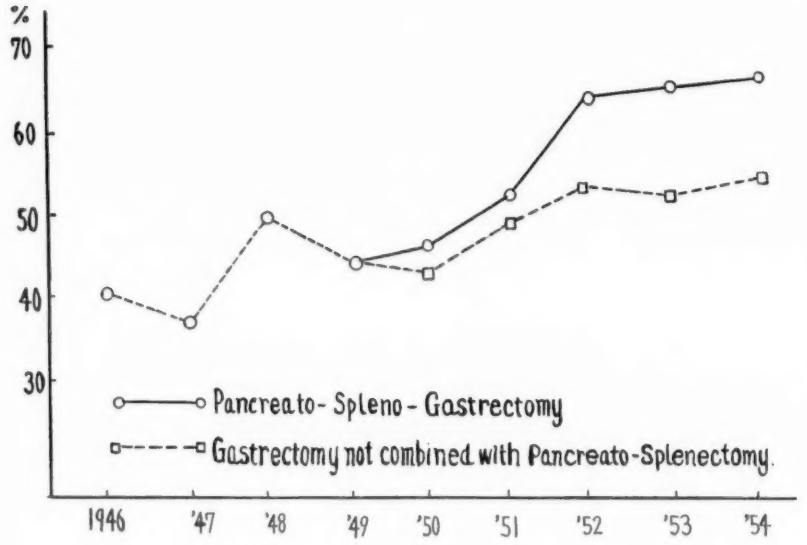


Fig. 11.

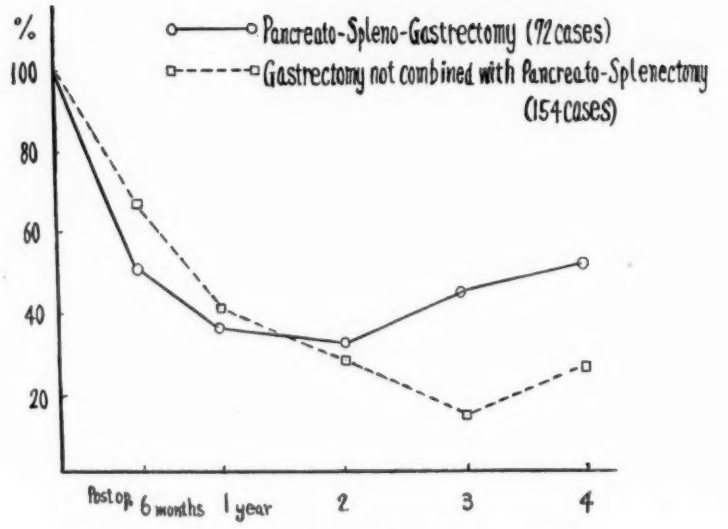


Fig. 12.

Fig. 11.—Operability of thoracic esophageal and cardiac cancer (January, 1946, to December, 1954).
Fig. 12.—Survival rate (January, 1950, to December, 1954).

tive day due to a leak at the anastomosis in the thorax, and another died on the ninth postoperative day of peritonitis due to a leak at the suture line. No causative factors attributable to splenectomy itself were ever noted. The period of postoperative hospitalization averaged thirty-three days each for 113 patients.

*Operative Rate.*—Those patients with cardiac cancer who have been treated by pancreatosplenogastrectomy since 1950 were compared with those treated solely by gastrectomy during the same period. According to this

TABLE IV. SURVEY ON OPERATIVE DETAILS IN PANCREATOSPLENOGASTRECTOMY PERFORMED IN THE NAKAYAMA SURGICAL DEPARTMENT FROM APRIL, 1950, TO MARCH, 1955

| | OPERATIVE METHOD | NO. OF CASES | NO. OF CASES | PANCREATO-SPLENECTOMY | SPLENEC-TOMY |
|---|---|---|---|---|---|
| Cardiectomy | Antethoracic esophagogastrostomy | 1 | 42 | 1 | 0 |
| | Intrathoracic esophagogastrostomy | 21 | | 21 | 0 |
| | Intra-abdominal esophagogastrostomy | 20 | | 19 | 1 |
| Total gastrectomy | Antethoracic esophagojejunostomy | 1 | 68 | 1 | 0 |
| | Intrathoracic esophagojejunostomy | 14 | | 13 | 1 |
| | Intrathoracic esophagojejunostomy (transplantation) | 9 | | 9 | 0 |
| | Intra-abdominal esophagojejunostomy | 21 | | 21 | 0 |
| | Intra-abdominal esophagojejunostomy (transplantation) | 16 | | 16 | 0 |
| | Intra-abdominal esophagoduodenostomy (end-to-end) | 7 | | 7 | 0 |
| Gastrectomy | Subtotal gastrectomy | 1 | 3 | 0 | 1 |
| | Partial gastrectomy | 2 | | 0 | 2 |
| Total | | | 113 | 108 | 5 |

TABLE V. OPERATIVE MORTALITY RATE FROM APRIL, 1950, TO MARCH, 1955

| OPERATIVE METHOD | NO. OF CASES | NO. OF DEATHS | OPERATIVE MORTALITY (PER CENT) |
|---|---|---|---|
| Pancreatosplenogastrectomy | 113 | 2 | 1.77 |
| Gastrectomy not combined with pancreatosplenectomy | 238 | 7 | 2.94 |

study, the operative rate was found to have been improved up to 65 per cent (Fig. 11). On the other hand, inoperability in radical treatment was investigated. The main reason that a radical cure was not feasible before application of this operative method was that retroperitoneal infiltration (including the pancreas and the spleen) is an early occurrence in these carcinomas. In comparison with an inoperability rate of 24 per cent prior to 1950 when the procedure was not yet adopted in our clinic, its inoperability since 1950 is as low as 10 per cent. Thus, this operative procedure has enlarged the limits of a radical cure in cancer of the cardia.

*Follow-up Results.*—This survey includes 72 patients who underwent pancreatosplenogastrectomy during a period from 1950 to December, 1954. An interesting fact to us is that their survival rate after the elapse of one year is higher than that of the controls, which indicates a superiority of this operative procedure (Tables VI and VII and Fig. 12).

TABLE VI. SURVEY ON SURVIVAL PERIOD AND RATE OF PATIENTS UNDERGOING PANCREATOSPLENOGASTRECTOMY IN THE NAKAYAMA SURGICAL DEPARTMENT FROM JANUARY, 1950, TO JUNE, 1955

| | JAN. 1, 1950 TO DEC. 31, 1950 | JAN. 1, 1951 TO DEC. 31, 1951 | JAN. 1, 1952 TO DEC. 31, 1952 | JAN. 1, 1953 TO DEC. 31, 1953 | JAN. 1, 1954 TO JUNE 30, 1954 | TOTAL | PER CENT |
|---|---|---|---|---|---|---|---|
| No. of cases | 2 | 8 | 24 | 24 | 17 | 75 | |
| Operative deaths | 0 | 0 | 1 | 1 | 0 | 2 | |
| No. of cases not followed | 0 | 1 | 0 | 0 | 0 | 1 | |
| No. of cases followed | 2 | 7 | 23 | 23 | 17 | 72 | |
| 6 Months | 1 | 5 | 14 | 10 | 7 | 37 | 51.39 |
| 1 Year | 1 | 3 | 9 | 7 | | 20 | 36.36 |
| 2 Years | 1 | 3 | 6 | | | 10 | 31.25 |
| 3 Years | 1 | 3 | | | | 4 | 44.44 |
| 4 Years | 1 | | | | | 1 | 50.00 |

TABLE VII. SURVEY ON SURVIVAL PERIOD AND RATE OF PATIENTS UNDERGOING GASTRECTOMY NOT COMBINED WITH PANCREATOSPLENECTOMY IN THE NAKAYAMA SURGICAL DEPARTMENT FROM JANUARY, 1950, TO JUNE, 1955
(CARDIECTOMY [INTRATHORACIC OR INTRA-ABDOMINAL] PLUS TOTAL GASTRECTOMY)

| | JAN. 1, 1950 TO DEC. 31, 1950 | JAN. 1, 1951 TO DEC. 31, 1951 | JAN. 1, 1952 TO DEC. 31, 1952 | JAN. 1, 1953 TO DEC. 31, 1953 | JAN. 1, 1954 TO JUNE 30, 1954 | TOTAL | PER CENT |
|---|---|---|---|---|---|---|---|
| No. of cases | 17 | 41 | 55 | 38 | 19 | 170 | |
| Operative deaths | 0 | 0 | 4 | 0 | 0 | 4 | |
| No. of cases not followed | 1 | 1 | 3 | 5 | 2 | 12 | |
| No. of cases followed | 16 | 40 | 48 | 33 | 17 | 154 | |
| 6 Months | 9 | 32 | 23 | 23 | 14 | 101 | 65.6 |
| 1 Year | 6 | 22 | 12 | 18 | | 58 | 42.3 |
| 2 Years | 8 | 9 | 8 | | | 25 | 24.0 |
| 3 Years | 4 | 4 | | | | 8 | 14.0 |
| 4 Years | 4 | | | | | 4 | 25.0 |

## CONCLUSION

Gastrectomy with pancreatosplenectomy for cancer of the stomach is presented with a tabulation of experimental studies regarding the incidence of splenic nodes with cancer and animal experiments for pancreatic function and histology.

It is our belief that this operative method should be used more extensively for appropriate cases.

## REFERENCES

1. Brunschwig, A.: Cancer **1**: 427, 1948.
2. Brunschwig, A.: Ann. Surg. **141**: 62, 1955.
3. Delannoy, E.: Mém. Acad. chir. **74**: 762, 1948.
4. Finsterer, H.: Deutsche Ztschr. Chir. **273**: 611-682, 1953.
5. Karcher, H.: Deutsche Ztschr. Chir. **279**: 384, 1954.
6. Nakayama, K.: Chirurg. **26**: 277, 1955.
7. Sweet, R.: Ann. Surg. **138**: 297, 1953.

# PANCREATIC FUNCTION STUDIES BEFORE AND AFTER THORACOLUMBAR SYMPATHECTOMY AND SPLANCHNICECTOMY FOR CHRONIC RELAPSING PANCREATITIS

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NOT only is the etiology of chronic relapsing pancreatitis uncertain but the methods of treatment vary widely. Medical therapy which includes, in the main, a high protein, high caloric diet, vitamins, antispasmodics, and pancreatic supplements is usually unsuccessful. Ultimately the incapacitating abdominal pain and/or weight loss plus the inability to perform daily work brings the patient to the surgeon. This picture is too often overshadowed by narcotic addiction. Most surgeons agree that the primary step is cholecystectomy if biliary calculi are present. Beyond this all agreement ends. The numerous methods of treatment underscore the basic differences concerning the etiology of the disease process. In the main there are two major avenues of surgical approach in addition to correction of the primary biliary tract disease. One is a direct attack on the pancreas itself, which includes pancreaticoduodenectomy, partial or total pancreatectomy, pancreaticolithotomy, ligation of the pancreatic duct, and caudal pancreatico-docho-jejunostomy. The second includes the various indirect procedures such as biliary tract drainage, diversion of the biliary stream from the area of the sphincter of Oddi, sphincterotomy, operations designed to decrease stimulation of pancreatic secretion (i.e., vagotomy, subtotal gastrectomy), and finally sympathectomy and/or splanchnicectomy.

In 1945 Mallet-Guy, Jean Jean, and Serretaz[7] reported 11 cases of unilateral subdiaphragmatic splanchnicectomy for relief of pain from chronic pancreatitis. This was followed in 1950 by a report[8] of 70 patients treated in a similar manner with 83 per cent showing improvement after the operation. Smithwick[4] reported a good result after six months following a transthoracic resection of the sympathetic trunk on the right side from $D_3$ to $D_{12}$ inclusive with the greater splanchnic nerve. Since then there have been many additional reports[1-3, 5, 6] of small groups of patients with favorable results from 3 to 14 months after sympathectomy. Ray and Console,[12] after rather extensive studies, have concluded that pain sense from the pancreas is mediated by visceral afferent nerves that traverse the celiac plexus, the splanchnics, and the sym-

Received for publication Sept. 14, 1955.

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pathetic chains on both sides. The vagus nerves play no part in the transmission of pain sense from the pancreas. Ray has proposed that the minimal operation to provide total analgesia of the pancreas is resection of the ganglionated chains from $T_{11}$ to $L_1$ on both sides and the lowest 8 cm. of the greater splanchnic nerves. Bingham, Ingelfinger, and Smithwick[1] feel that unilateral sympathectomy will occasionally relieve intractable pancreatic pain because of elevation of the pain threshold.

Since 1949 there have been 5 patients on our service who have had transthoracic thoracolumbar sympathectomy and splanchnicectomy for intractable pain resulting from chronic relapsing pancreatitis. With the introduction of the secretion-duodenal drainage test we felt we had a unique opportunity of studying the exocrine function of the pancreas both pre- and postoperatively in these patients. The technique used has been previously described.[9] Briefly, a double-lumen Einhorn tube is placed into the duodenum under fluoroscopic control to rest just proximal to the ligament of Treitz. The duodenal juice is collected for twenty minutes as a resting sample. Following this, one clinical unit of the hormone secretin* per kilogram of body weight is given intravenously and an eighty minute collection period is carried out. The specimen is analyzed for volume produced, maximal bicarbonate concentration, and the amount and concentration of enzyme, notably amylase in these studies. Reyes[13] and Gage[4] believe that this operation, besides relieving pain, might have a direct therapeutic effect on the disease process by relieving ductal and vascular spasm. Popper, Necheles, and Russell[10] converted edematous pancreatitis into necrotic pancreatitis by temporary occlusion of the main arterial supply. It was our purpose to learn whether this operation could possibly result in physiologic improvement of pancreatic function as well as abate pain in cases of chronic relapsing pancreatitis. Accordingly, 4 patients were examined preoperatively by the secretin-duodenal drainage test and the values for the volume, bicarbonate concentration, and amylase produced fell into the diagnostic range of chronic pancreatitis thereby confirming the clinical impression. All 4 patients were examined again by similar technique an average of 2 years, 2 months postoperatively and pancreatic function was compared to preoperative levels. A fifth patient included in this study was operated upon Oct. 20, 1949, for pancreaticolithiasis associated with intractable abdominal pain. He had his first secretin test one and one-half years postoperatively in March, 1951, when we first undertook the study and these results were compared with results 4 years later. In all 12, separate secretin-duodenal drainage tests were performed. Each patient was followed closely in the interim between tests and checked for possible complications.

## CASE REPORTS

CASE 1.—(Bellevue Hospital No. 67117-49.) R. L., a 52-year-old white man, entered the hospital Sept. 1, 1949, complaining of severe, sharp postprandial epigastric pain and slight burning type pain before eating associated with weight loss, anorexia, and weakness present for two years.

*Supplied by Eli Lilly and Company, Indianapolis, Indiana.

The patient first became ill about 9 years prior to admission at which time he noted burning epigastric pain coming on about one-half hour prior to meals, relieved by food or alkali. He also noted a weight loss of about 30 pounds. At another hospital he was told a gastrointestinal series revealed a duodenal ulcer. He was given some injections in the hospital and a diet of milk and eggs. He regained most of his weight and was discharged on a diet of milk and soft foods. Prior to his illness he had been consuming about one quart of whiskey per day and smoking about one pack of cigarettes a day. Following discharge from hospital he didn't smoke or drink and had no more pain.

Seven years prior to admission he started to drink about a pint of whiskey a day and a year later was admitted to Bellevue Hospital for the first time. Work-up at that time failed to reveal a peptic ulcer or other gastrointestinal abnormality. He remained well on a bland diet with only an occasional alcoholic drink. Two years before admission he again developed epigastric pain, somewhat greater on the right side, which continued intermittently in spite of a bland diet and abstinence from alcohol. In that period he lost 25 to 30 pounds associated with anorexia and weakness. On admission he noted a burning pain before meals and a sharper type of pain coming on about one-half hour after meals occasionally relieved by sitting or standing. He had no nausea or vomiting. Bowel movements were regular.

Physical examination revealed a poorly nourished man in chronic distress. Blood pressure was 104/66. There was some epigastric tenderness just to the right of the midline but otherwise findings were negative. Laboratory results: white blood cells, 8,900; polycytes, 51 per cent; lymphocytes, 46 per cent; monocytes, 2 per cent; eosinophils, 1 per cent; red blood cells, 4,540,000. Hemoglobin 13 Gm., urinalysis normal, sugar 129, nonprotein nitrogen 32, total proteins 7, albumin-globulin ratio 4.5/1.5, alkaline phosphatase 1.7, acid phosphatase 0.7, serum amylase 6.4, 4.4 (normal values 1.0-2.5), serology negative. Stool for fat, 29.8 per cent neutral fat, fatty acids, and soap. Two separate gastrointestinal series were normal. There was diffuse calcification involving the entire pancreas. Gall-bladder series was normal.

On Oct. 20, 1949, a right thoracolumbar sympathectomy and splanchnicectomy ($T_6$ to $L_3$) was carried out. His postoperative course was uneventful and he was discharged in eleven days. The patient weighed 109 pounds at the time of operation and now weighs 129 pounds. He is free of abdominal pain and is gainfully employed. He still admits to a "moderate" alcoholic intake. No diabetes is present. He remains normotensive.

*Secretin-duodenal drainage tests:*

| | March 14, 1951 | April 15, 1955 |
|---|---|---|
| Total Volume: | 63 c.c. | 71 c.c. |
| Maximum $HCO_3$ concentration: | 31.4 meq./L. | 26.2 meq./L. |
| Total Amylase: | | |
| Pre-injection | 0 | 0 |
| 0-20 Minutes | 18.5 Units | 10.5 Units |
| 20-80 Minutes | 34.2 Units | 37.1 Units |

CASE 2.—(University Hospital K84357.) A. S., a 42-year-old white woman, was admitted Nov. 23, 1951, with a history of bouts of sharp, noncolicky abdominal pain. The pain was mainly subcostal, somewhat more severe on the left, and unrelated to meals or seasons. No nausea or vomiting was present. Bowel movements were regular. She admitted to being a "moderate" alcoholic drinker.

Since onset the attacks of pain became increasingly intense and she had become addicted to opiates. Although there was no anorexia the patient had lost 15 pounds of weight. She had been to numerous physicians and had many hospital admissions in the course of which a series of gastrointestinal and gall-bladder examinations, intravenous pyelograms, and barium enemas were performed without any positive findings. She had been labelled psychoneurotic by several physicians. At another hospital a possible left nephrectomy had been advised.

Physical examination revealed a thin female in moderately acute distress perfectly free of complaints after an injection of Demerol. Blood pressure was 130/90. The abdomen

was soft and flat with some tenderness in the epigastrium. Otherwise findings were normal. Laboratory results: white blood cells 9,750, polycytes 59 per cent, lymphocytes 30 per cent, monocytes 7 per cent, eosinophils 4 per cent. Red blood cells 3,540,000, hemoglobin 11.1 Gm., urinalysis, 3 + acetone, otherwise normal, serum amylase 13.2 (normal 1.0-2.5), blood urea nitrogen 8, sedimentation rate 101.

On Nov. 26, 1951, an exploratory laparotomy was performed. The patient was found to have a chronic pancreatitis involving the entire gland and a biopsy from the body was taken. Accordingly the abdominal wound was closed and the patient was placed on her right side and a left thoracolumbar sympathectomy and splanchnicectomy ($T_5$ to $L_3$) was performed. The pancreatic biopsy revealed interstitial fibrosis consistent with the diagnosis of chronic pancreatitis. The patient was discharged seventeen days postoperatively after an uneventful course.

She was readmitted on April 2, 1952, with a history of three days' intermittent, crampy-type right upper quadrant pain requiring morphine, codeine, and Banthine for control. She felt nauseated but did not vomit. This was the second bout of such abdominal pain since her first operation. Serum amylase was 2.1. On April 7, 1952, a right-sided thoracolumbar sympathectomy and splanchnicectomy ($T_6$ to $L_3$) was carried out. She was discharged asymptomatic thirteen days postoperatively and has been followed closely since that time. When she underwent her first operation she weighed 85 pounds. She now weighs 100 pounds. She has had no attacks of abdominal pain since her second operation and has overcome her addiction to opiates. She continues to admit to a "moderate" alcoholic consumption and is gainfully employed. In all this patient has had 4 separate secretin tests.

*Secretin-duodenal drainage tests:*

| | December 4, 1951 | April 4, 1951 | August 22, 1952 | January 28, 1955 |
|---|---|---|---|---|
| Total Volume: | 33 c.c. | 52 c.c. | 109 c.c. | 100 c.c. |
| Maximum $HCO_3$ concentration: | 27.3 meq./L. | 39.2 | 36 | 47 |
| Total Amylase: | | | | |
| Pre-injection | No specimen | | 37.3 Units | 0 |
| 0-20 Minutes | 27.3 Units | 3.92 | 36.6 Units | 4.2 |
| 20-80 Minutes | 24.1 Units | 68.9 | 173.0 Units | 6.0 |

CASE 3.—(University Hospital K86687.) R. R., a 56-year-old woman, was admitted April 20, 1953, with a history of intermittent epigastric and right upper quadrant pain radiating to the back associated with nausea, vomiting, and occasional jaundice for three years. In 1950 she had a cholecystectomy at another hospital for presumable biliary calculi. Since then the patient experienced 3 to 6 yearly episodes of jaundice, clay-colored stools, and dark urine with bouts of right upper quadrant and epigastric pain. On two occasions she had fever and chills with these attacks. She was having a typical attack when admitted. There had been a 25 pound weight loss in the past six months. Her appetite was poor. Bowel movements had been somewhat bulky and excessively odorous.

Physical examination revealed a woman in acute distress. Blood pressure was 130/80. Pulse was 80. Temperature was 102° F. There was moderate tenderness in the epigastrium and right upper quadrant with spasm of the upper abdominal musculature. Healed upper right rectus and McBurney incisions were present. No other abnormal findings were noted. Laboratory results: white blood cells 20,450, polycytes 83 per cent (many stabs), lymphocytes 11 per cent, monocytes 4 per cent, metamyelocytes 2 per cent, red blood cells 3,400,000, hemoglobin 9.8 Gm., urinalysis, negative except for 1 plus sugar and bile present, serum amylase 17.8 (normal 1.0-2.5), sugar 200, alkaline phosphatase 14.6, icterus index 24.6, total cholesterol 140, esters 75, esters/total 53 per cent, prothrombin time 50 sec. (normal 36-45 sec.). Flat and erect x-ray films of the abdomen were negative.

She was treated conservatively with Levine tube suction, intramuscular Banthine, intravenous fluids, analgesics, and antibiotics and responded within forty-eight hours. A secretin test on April 23 confirmed the clinical impression of chronic pancreatitis. On April 27 an exploratory laparotomy was carried out. The region of the head of the pancreas was markedly enlarged and indurated. The common duct was found to be dilated but exploration failed to reveal calculi. A No. 18 T tube was inserted into the common duct. No biopsy was taken from the pancreas because of the recent bout of pancreatitis. Postoperatively a cholangiogram revealed the dye to pass readily into the duodenum. The patient ran an unexplained febrile course for thirteen days but finally became afebrile and on May 14, 1953, a bilateral thoracolumbar sympathectomy and splanchnicectomy ($T_{12}$ to $L_2$) plus the excision of celiac ganglia and lower three inches of the greater splanchnic nerves was performed. Postoperatively she did well except for moderate incisional pain. On May 29 the T tube was removed after a second cholangiogram showed good visualization of the common and hepatic ducts and rapid emptying of the dye into the duodenum. The patient was discharged twenty-one days after her operation.

She has been followed by us and her only subjective complaint is some left subcostal pain which comes on after eating grapes, raisins, or prunes. Otherwise she is free of pain. She continues to work daily as a proofreader on one of the large metropolitan newspapers. Her weight had increased from 128 pounds at the time of her original operation to 155 pounds when last seen. Up to 20 units of Protamine Zinc Insulin daily had been required to control her diabetes but for the last three months she has used no insulin. Her blood pressure remains at 130/70. This patient does not drink alcoholic beverages.

*Secretin-duodenal drainage tests:*

| | April 23, 1953 | April 23, 1955 |
|---|---|---|
| Total Volume: | 87 c.c. | 31 c.c. |
| Maximum $HCO_3$ concentration: | 70.4 meq./L. | 9.9 meq./L. |
| Total Amylase: | | |
| Pre-injection | 5.5 Units | No Specimen |
| 0-20 Minutes | 44.3 Units | 7.0 Units |
| 20-80 Minutes | 18.9 Units | 5.0 Units |

CASE 4.—(University Hospital K85328—Patient of Dr. S. Arthur Localio.) M. P., a 49-year-old white woman, entered the hospital June 1, 1953, complaining of abdominal pain of six months' duration. In December, 1952, she experienced her first severe attack of left upper quadrant pain following a heavy meal. She described the pain as boring through into the back with some radiation to the left shoulder. These pains continued intermittently despite various dietary and antispasmodic therapy. There was nausea and some anorexia present but no vomiting. In the six-month period she had lost 16 pounds. Opiate injections were given by the local physician on several occasions to relieve the pain. Two separate gastrointestinal and gall-bladder series were reported as being negative.

Physical examination revealed a somewhat apprehensive woman in no apparent distress. Blood pressure was 120/90. Except for some tenderness in the left upper quadrant near the midline and the question of a deeply palpable mass in this region examination was normal. Laboratory results: white blood cells 6,400, polycytes 51 per cent, lymphocytes 43 per cent, monocytes 3 per cent, eosinophils 3 per cent. Red blood cells 4,040,000, hemoglobin 11.2 Gm., urinalysis, negative. Sedimentation rate 16, serum amylase 1.9, lipase 0.45 (normal less than 1.0) glucose tolerance test normal. Sigmoidoscopy to five and one-half inches was negative as was a barium enema. A secretin test confirmed the clinical impression of chronic relapsing pancreatitis.

On June 12, 1953, an exploratory laparotomy was performed which was negative except for a thickening and chronic inflammation and fibrosis of the pancreas. A biopsy of the pancreas was taken. The abdominal wound was closed and the patient was turned into the right lateral position. A left thoracolumbar sympathectomy and splanchnicectomy ($T_7$ to $L_2$)

with excision of the greater, lesser, and least splanchnic nerves and celiac ganglion was carried out. The pancreatic biopsy revealed marked interstitial fibrosis consistent with the diagnosis of chronic pancreatitis. Eleven days postoperatively the patient was discharged after an uneventful course.

She is steadily employed as a textile-machine operator and suffers no abdominal pain. Eating a large meal gives her some vague epigastric discomfort but no pain. She remains 8 pounds below her preoperative weight in spite of a good appetite. No diabetes is present. There have been no hypotensive episodes. The patient does not drink alcohol.

*Secretin-Duodenal Drainage Tests:*

| | June 5, 1953 | March 8, 1955 |
|---|---|---|
| Total Volume: | 121 c.c. | 47 c.c. |
| Maximum $HCO_3$ concentration: | 29.7 meq./L. | 6.6 meq./L. |
| Total Amylase: | | |
| Pre-injection | 0.4 Unit | 0 |
| 0-20 Minutes | 181.9 Units | 4.6 Units |
| 20-80 Minutes | 54.1 Units | 28.1 Units |

CASE 5.—(University Hospital K86952.) C. A., a 49-year-old white woman, entered the hospital for the first time on Jan. 31, 1954, complaining of severe left upper quadrant pain of three days' duration. She dated the onset of her illness to two years previously when she began to notice bloating, belching, and right upper quadrant distress, most severe after eating "greasy" foods. Cholescystograms revealed calculi and eight days prior to admission she underwent a cholecystectomy. Her postoperative course was marked by left abdominal pain which increased in intensity and was severe enough to require 75 mg. of Demerol every six to eight hours for three days. She had taken small amounts of food and had no nausea or vomiting. One bowel movement was described as light yellow and urine had been dark. The patient had not been transfused during surgery. Temperatures had varied from 100 to 101° F. without any spikes or associated chills.

Physical examination revealed a questionably jaundiced woman in acute distress, somewhat lethargic from previous injection of Demerol. Blood pressure was 125/90. Pulse was 140, regular and full. Temperature was 101.8° F. Positive findings were limited to the abdomen which was moderately distended with tenderness and spasm of the left rectus musculature. There was rebound and referred rebound to the left upper quadrant but no rigidity. Both flanks were bulging with a suggestion of a fluid wave present. No organs or masses were palpable. Bowel sounds were absent. There was a cleanly healing upper right rectus incision with silk sutures in place. Laboratory results: white blood cells 24,100, polycytes 92 per cent, lymphocytes 7 per cent, monocytes 1 per cent. Red blood cells 5,700,000, hemoglobin 16.2 Gm., urinalysis revealed specific gravity of 1.034, protein 1+, and presence of bile. Serum amylase 10 (normal 1.0-2.5), blood urea nitrogen 17.5, sodium 123, potassium 5.25, chlorides 93, bicarbonate 20.9, bilirubin 2.8, icteric index 35.

She was treated conservatively with intramuscular Banthine, intravenous fluids, analgesics, antibiotics, and vitamin K. Because of lack of vomiting she was not put on Levine tube suction and allowed to take small amounts of fluid by mouth. After three days of this therapy she appeared much worse. Blood pressure was 110/80, pulse 130 to 140, and respirations 36 to 40. The abdomen was more distended and tympanitic with generalized tenderness and rebound. At this time she was placed on nothing by mouth, and a Kaslow tube was inserted into the stomach. One hundred fifty c.c. of bilious fluid was obtained. In addition it was felt that cortisone might be of definite value and accordingly she received 100 mg. intramuscularly as an initial dose and 50 mg. q. i. d. for two days. Improvement was dramatic after institution of this therapy. Within forty-eight hours her abdomen was softer with bowel sounds present. On February 6 she took oral fluids quite well and three days later was able to be discharged.

On March 14, 1954, she was admitted for the second time having experienced, six days prior to admission, her first attack of left upper quadrant pain since discharge. Following

this episode she had three other attacks of right upper quadrant pain which radiated through to the back. Demerol injections were required on each occasion to control the pain and she took Demerol freely between attacks. There was no nausea, vomiting, chills, fever, pruritus, or known jaundice although two stools had appeared somewhat light and the urine dark. Serum amylase was 2.2, alkaline phosphatase, 13.8, and icteric index 32.1. A secretin test on March 16 confirmed the clinical impression of a possible chronic relapsing pancreatitis. March 19 an exploratory laparotomy was carried out. A definite chronic pancreatitis was present. The common duct was not dilated. A choledochostomy failed to reveal the presence of calculi or malignancy. A No. 14 T tube was placed into the common duct and the abdomen was closed. The patient was turned into the lateral position and a right sympathectomy and splanchnicectomy ($T_{10}$ to $L_2$) was performed with excision of the greater, lesser, and least splanchnic nerves including the celiac ganglion. A postoperative cholangiogram showed a normal appearance of the hepatic and common ducts. The T tube was removed six days postoperatively and the patient continued to drain bile rather profusely. This fistula gradually closed and the patient was discharged April 12, 1954.

She has done remarkably well clinically. Her diet is unrestricted and there is no abdominal pain. She has gained 60 pounds in weight since her operation, having weighed 180 pounds when last seen. She freely admitted having been addicted to Demerol because of pain prior to each operation. This habit has been broken. She works steadily and remains normotensive. There is no diabetes present. She does not drink alcohol.

*Secretin-duodenal drainage tests:*

| | March 16, 1954 | May 2, 1955 |
|---|---|---|
| Total Volume: | 37.5 c.c. | 123 c.c. |
| Maximum $HCO_3$ concentration: | 58.2 meq./L. | 72.6 meq./L. |
| Total Amylase: | | |
| Pre-injection | No specimen | 28.8 Units |
| 0-20 Minutes | 8.0 Units | 14.4 Units |
| 20-80 Minutes | 41.4 Units | 155.5 Units |

*Normal secretin test values:*

| | |
|---|---|
| Total Volume: | 85-260 c.c. |
| Maximum $HCO_3$ concentration: | 90-210 milliequivalents per liter |
| Total Amylase: | |
| Pre-injection | 20-285 Lagerlof Units |
| 0-20 Minutes | 70-880 Lagerlof Units |
| 20-80 Minutes | 280-1050 Lagerlof Units |

## DISCUSSION

These 5 cases represent rather typical cases of chronic relapsing pancreatitis. One patient was thought to be psychoneurotic because of her bizarre symptomatology and lack of physical findings. Two patients had previous cholecystectomies as the initial treatment of their disease. Another patient was a chronic alcoholic who had suffered two years with intractable abdominal pain before a definite diagnosis could be made. In addition 2 of these patients were addicted to opiates. Except for Case 1 where pancreaticolithiasis was present the 4 remaining patients were subjected to exploratory laparotomy to confirm the diagnosis established by clinical impression and secretin studies as well as to definitely rule out any biliary tract pathology. All had an enlarged, firm, indurated pancreas, 3 with involvement of the entire gland and 1 with involvement of the head alone. Biopsies which were taken in Cases 2 and 4 revealed interstitial fibrosis consistent with the diagnosis of chronic relapsing pancreatitis.

Two patients had bilateral and 3 patients had unilateral thoracolumbar sympathectomies and splanchnicectomies for relief of their intractable abdominal pain. Two of the unilateral operations were on the right side and one was on the left, that being the side of greatest pain. The earliest operations involved removal of the ganglionated chain from $T_6$ through $L_3$ inclusive plus the splanchnic nerves. More recently a more limited type of operation extending from $T_{10}$ to $L_2$ with removal of the greater, lesser, and least splanchnic nerves and the celiac ganglion has been carried out.

All 5 patients are clinically well after an average postoperative follow-up of three years. Case 1 is now 6 years postoperative with an excellent result for diffuse pancreaticolithiasis. None of the patients has any abdominal pain typical of the pain present prior to operation. All 5 are gainfully employed. There has been an average weight gain of 33 pounds in 4 patients while the other has lost 8 pounds since operation. The 2 patients who were addicted to narcotics are now free of the habit. Case 3 had diabetes which required up to 20 units of Protamine Zinc Insulin daily, but which, in the last three months of follow-up, had been controlled on diet alone. None of the other cases developed diabetes. There has been no x-ray evidence of the development of pancreaticolithiasis and none of the cases have been complicated by pseudocyst formation. Finally it should be mentioned that "moderate" alcoholic intake persists in Cases 1 and 2 by their own admission yet they continue to stay well.

Secretin-duodenal drainage tests were performed an average of two years and two months postoperatively in Cases 2, 3, 4, and 5 and four years following the initial test in Case 1. This enabled us to compare our subjective impressions with some objective findings. In 3 cases there was a diminution of exocrine function of the pancreas in response to the hormone secretin. One case remained approximately the same, showing similar low values for volume of juice collected, maximum bicarbonate concentration, and the amount and concentration of amylase. Only in Case 5, which has the shortest follow-up, has there been an improvement in exocrine pancreatic function after unilateral sympathectomy, splanchnicectomy, and celiac ganglionectomy. It is interesting that Case 2 showed a temporary improvement in pancreatic function eight months after operation only to show a marked decline two and one-half years later.

This series of 5 cases is too small to draw any definite conclusions. However, as a preliminary observation it can be noted that thoracolumbar sympathectomy and splanchnicectomy seems to have little effect on the progression of the disease process in chronic pancreatitis. That this depression of exocrine function of the pancreas is an unwanted feature cannot be stated. Some operations (i.e., vagotomy, subtotal gastrectomy) for the alleviation of chronic relapsing pancreatitis are designed to diminish the response of the pancreas to stimulation by secretin. We will continue to follow patients that have been operated upon more recently as well as these cases and perhaps have a more conclusive report at a later date.

SUMMARY

1. Five consecutive patients have been treated by thoracolumbar sympathectomy and splanchnicectmoy (2 bilateral, 3 unilateral) for the relief of intractable abdominal pain resulting from chronic relapsing pancreatitis.

2. After an average postoperative follow-up of three years all 5 patients are clinically well and free of abdominal pain.

3. A study of the exocrine function of the pancreas has been made in these patients pre- and postoperatively by the secretin-duodenal drainage test. Three patients exhibit a decline in the response of the pancreas to the hormone secretin while one patient shows slightly improved pancreatic function after an average follow-up of two years and two months. A fifth patient remains essentially unchanged four years between secretin tests.

REFERENCES

1. Bingham, J. R., Ingelfinger, M. D., and Smithwick, R. H.: The Effect of Sympathectomy on Abdominal Pain in Man, Gastroenterology **15:** 18-33, 1950.
2. Connolly, J. E., and Richards, V.: Bilateral Splanchnicectomy and Lumbodorsal Sympathectomy for Chronic Relapsing Pancreatitis, Ann. Surg. **131:** 58-63, 1950.
3. de Takats, G., Walter, C. E., and Lasner, J.: Splanchnic Nerve Section for Pancreatic Pain, Ann. Surg. **131:** 44-57, 1950.
4. Gage, M., and Gillespie, G.: Acute Pancreatitis and Its Treatment, South. M. J. **44:** 769-772, 1951.
5. Hurwitz, A., and Gurwitz, J.: Relief of Pain in Chronic Relapsing Pancreatitis by Unilateral Sympathectomy, Arch. Surg. **61:** 372-378, 1950.
6. Hyman, H. L., and Burton, C. C.: Treatment of Chronic Relapsing Pancreatitis by Sympathectomy and Splanchnicectomy, Gastroenterology **18:** 43-48, 1951.
7. Mallet-Guy, P., Jean Jean, R., and Serretaz, P.: Distant Results in the Treatment of Chronic Pancreatitis by Unilateral Splanchnicectomy, Lyon Chir. **40:** 293-300, 1945.
8. Mallet-Guy, P., and Beaujeu, M. J.: Treatment of Chronic Pancreatitis by Unilateral Splanchnicectomy, Arch. Surg. **60:** 233-241, 1950.
9. Pfeffer, R. B., Stephenson, H. E., Jr., and Hinton, J. W.: The Effect of Thoracolumbar Sympathectomy and Vagus Resection on Pancreatic Function in Man, Ann. Surg. **136:** 585-594, 1952.
10. Popper, H. L., Necheles, H., and Russell, K. C.: Transition of Pancreatic Edema into Pancreatic Necrosis, Surg., Gynec. & Obst. **87:** 79-85, 1948.
11. Rack, F. J., and Elkins, C. W.: Experiences With Vagotomy and Sympathectomy in the Treatment of Chronic Recurrent Pancreatitis, Arch. Surg. **61:** 937-943, 1950.
12. Ray, B. S., and Console, A. D.: The Relief of Pain in Chronic (Calcareous) Pancreatitis by Sympathectomy, Surg., Gynec. & Obst. **89:** 1-8, 1949.
13. Reyes, H.: Pancreatitis aguda y bloqueo anestésica del esplácnicosemilunar, Arch. Soc. cirujanos hosp. **15:** 723-727, 1945.
14. Smithwick, R. H.: Discussion of Paper of A. O. Whipple, Ann. Surg. **124:** 1006-1007, 1946.

# TRAUMATIC INJURIES OF THE PANCREAS

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PANCREATIC injuries resulting from external trauma are relatively uncommon, occurring in approximately 1 to 2 per cent of abdominal wounds. Case presentations appear periodically, but within the past ten years the largest series reported in the English literature from a civilian institution included only 17 patients. Few surgeons, therefore, have had the opportunity to treat a significant number of patients with trauma to this organ, for such injuries are infrequently seen even during military campaigns. This study was undertaken to review the experience with this lesion in the Baylor University affiliated hospitals where large numbers of patients with abdominal wounds are treated.

## MATERIAL

The records of 31 patients with injuries to the pancreas secondary to external trauma have been reviewed, the diagnosis in each instance having been confirmed at operation. Twenty-nine of these patients were treated at Jefferson Davis and Veterans Administration Hospitals during the fifteen-year period ending in 1955, while 2 were private patients.

Twenty-six injuries resulted from penetrating wounds, including 15 bullet wounds, 10 knife wounds and 1 shotgun blast. Two automobile accidents and 3 falls from ladders and horses accounted for 5 blunt injuries (Table I). The injuries involved all segments of the pancreas, being slightly more common in the head and tail (Table II). Injury to the pancreatic duct, though often suspected, was not identified at the time of operation.

The pancreas was the only viscus damaged in the patients with blunt injuries, but injury of associated organs was invariable when the pancreatic injury was of the penetrating type. Thus, there were only 5 patients in whom the pancreas was the only organ injured, while in 21 patients injuries involved 2 or more additional organs (Table III).

## TREATMENT AND RESULTS

Surgical management of the pancreatic wounds consisted of hemostasis and drainage. Débridement seemed feasible in only one instance where massive injury of the tail necessitated a caudal resection. The pancreatic duct was never visualized primarily, and the critical condition of the patients prohibited extensive dissection; therefore repair was not performed.

Five (16 per cent) of the 31 patients died. All deaths occurred within three days following injury, 80 per cent being within twenty-four hours. The wound in each instance was penetrating in type (1 shotgun, 1 knife, and 3 bullet wounds), and injuries to other organs and blood vessels were primarily responsible for the fatal outcome rather than the injury to the pancreas

Received for publication Sept. 2, 1955.

(Table I). Death resulted from hemorrhage in 4 patients (left renal artery; kidney and colon; aorta, vena cava and portal vein; and liver and duodenum), and postoperative aspiration in the fifth patient. Two and probably 3 of the deaths were preventable. The postoperative aspiration was preventable. Another patient died on the third day from an unrecognized injury to the renal artery and vein. The third patient who might have been saved received a shotgun blast to the abdomen, was explored, but continued to bleed, requiring a secondary laparotomy fourteen hours later. Bleeding had persisted from the many perforations of the colon and kidney. Death occurred a few hours after the second operation.

TABLE I. MORTALITY AS RELATED TO TYPE OF INJURY

| TYPE OF INJURY | WOUNDING AGENT | | NUMBER OF PATIENTS | MORTALITY (PER CENT) |
|---|---|---|---|---|
| Penetrating or perforating | | | 26 | |
| | Shotgun | 1 | | 100 |
| | Bullet | 15 | | 20 |
| | Knife | 10 | | 10 |
| Blunt | | | 5 | |
| | Automobile accident | 2 | | 0 |
| | Fall | 3 | | 0 |
| Total | | | 31 | 16 |

TABLE II. THE INCIDENCE OF PANCREATIC FISTULA ACCORDING TO LOCATION OF WOUND (PENETRATING TYPE)

| SITE OF INJURY | NUMBER OF PATIENTS | NUMBER DEVELOPING FISTULA |
|---|---|---|
| Head | 8 | 4* |
| Body | 5 | 1 |
| Tail | 8 | 1 |
| Total | 21 | 6 |

*Includes the only two patients with penetrating wounds who developed a prolonged drainage (40 and 64 days).

TABLE III. INCIDENCE OF ASSOCIATED INJURIES (PENETRATING WOUNDS)

| | | | |
|---|---|---|---|
| Liver | 12 | Lungs | 3 |
| Stomach | 11 | Spleen | 3 |
| Duodenum | 4 | Inferior vena cava | 2 |
| Kidney | 4 | Gall bladder | 1 |
| Colon | 3 | Rectum | 1 |
| Small bowel | 3 | Spinal cord | 1 |
| Major arteries | 3 | Portal vein | 1 |

Although death was due primarily to associated injuries, nonfatal complications were due primarily to the injury to the pancreas. Serum amylase studies indicate that pancreatitis, of at least a limited extent, is probably a characteristic sequel of pancreatic injury[14, 23] (Figs. 1 and 2). Thirty-five per cent of the 26 patients who survived developed pancreatic fistulas, 8 per cent developed cysts, and 4 per cent an abscess involving the head of the pancreas. These complications were relatively more frequent in the patients with blunt trauma, and it is noteworthy that both of the pancreatic cysts developed in this group (Table IV). Among the patients with penetrating injuries, pan-

creatic fistulas resulted most frequently from injuries of the head of the pancreas and from injuries due to bullet wounds in contradistinction to stab wounds (Table II). Six of the fistulas closed promptly, but 2 patients with penetrating wounds of the head of the pancreas had drainage for forty and

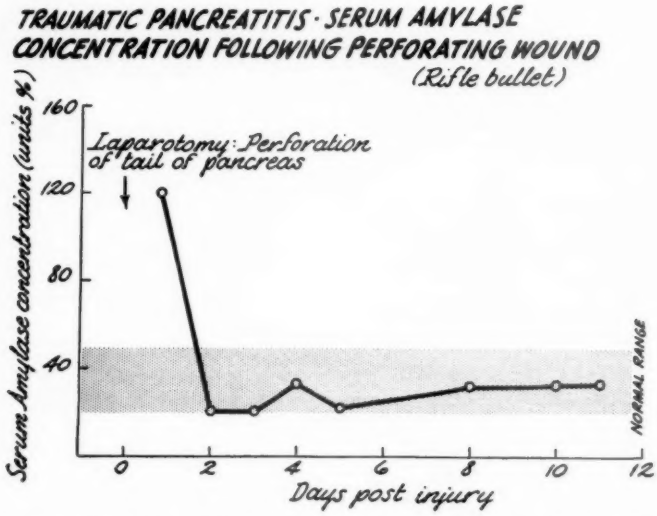


Fig. 1.—Demonstrating the short duration in the elevation of the serum amylase concentration following perforation of the tail of the pancreas.

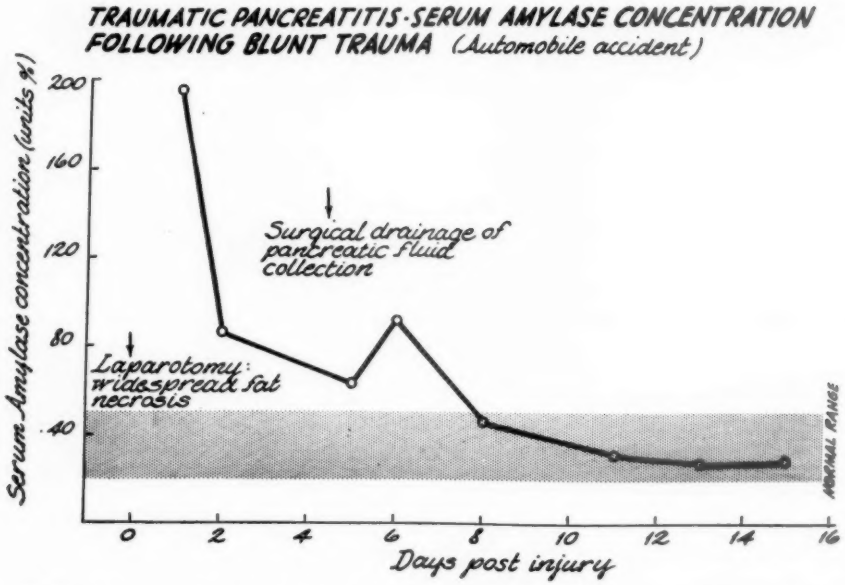


Fig. 2.—Following a crushing injury of the pancreas, the serum amylase concentration rose and remained elevated for a prolonged period.

sixty-four days, respectively. Another patient, following blunt trauma, developed a collection of pancreatic fluid which was drained surgically three days later and has since had a minor pancreatic fistula for fourteen months.

The longest period of hospitalization was sixty-eight days, necessitated by a pancreatic fistula, but most of the patients left the hospital within two weeks.

TABLE IV. INCIDENCE OF PANCREATIC COMPLICATIONS AS RELATED TO TYPES OF INJURY

| TYPE OF INJURY | NUMBER OF PATIENTS* | NUMBER WITH PANCREATIC FISTULA | NUMBER WITH PSEUDOCYST OF PANCREAS | NUMBER WITH ABSCESS |
|---|---|---|---|---|
| Penetrating injuries | 21 | 6 | 0 | 0 |
| Knife | 9 | 1 | – | – |
| Bullet | 12 | 5 | – | – |
| Blunt injuries | 5 | 3 | 2 | 1 |
| Total | 26 | 9 | 2 | 1 |

*Survivors.

## DISCUSSION

A relative newcomer among medical subjects, the first pancreatic injury was described slightly more than a century ago, in 1827, when the following report appeared in the *Lancet:*

> A case in which this singular accident occurred was brought to the Hospital during the last admission week of Mr. Travers. The patient, a woman in the state of intoxication, was knocked down by the wheel of a stage coach, which, however, we understand did not pass over her but violently struck against her, occasioning fracture of the ribs. She was taken to the Hospital and lived several hours after the accident.
>
> The pancreas, on examination of the body, was found to be completely torn through transversely; there was also laceration of the liver and extensive effusion of blood into the abdomen. The vena portae was uninjured.[34]

During the succeeding years, several other cases were reported. By 1876, 7 reports of pancreatic injury were collected from the literature by Otis,[24] who added 5 more, including both blunt and penetrating trauma. One reported by Kleberg[19] of Odessa was specified as a "60 year old discharged soldier, Anton Stepanowitch, who was stabbed when he fell among thieves." The protruding pancreas was ligated and excised, and, without subsequent fever or peritonitis, the patient left the hospital, cured, in twenty-one days.

In 1903, a collected series of 45 case reports was summarized by von Mikulicz[35] and comparable studies were reported by others during the ensuing decade.[9, 11] Von Mikulicz collected 9 nonfatal stab wounds of the pancreas, 7 of which presumably represented stabs in the back for they were without intra-abdominal injury.

In 1928, Schmeiden and Sebening[28] collected 62 cases of pancreatic injury from the European clinics. The mortality was 52 per cent. About the same time, Stern[30] compiled an extensive review of the literature.

Military experiences offer the most interesting historical description of the management of pancreatic injuries. Only 5 injuries of the pancreas were recorded in the Surgeon General's report of the American Civil War, 1861-1865. The mortality was 80 per cent. Death was due to peritonitis in one patient, secondary hemorrhage in the other 3. Laparotomy was not performed.

Case 506, from the Surgeon General's report, portrays the therapeutic hopelessness of the era:

> Case 506. Acting Assistant Surgeon Thaddeus L. Leavitt reports that Corporal Augustus B. Jones, Co. D, 5th Vermont, aged 27 years, was wounded at the battle of Wilderness, May 10, 1864, laid out on the battle field one day and night, was then removed to field hospital, from there carried by boat to Washington, and jolted over a rough road of two miles to the Lincoln Hospital, which he reached about two o'clock in the morning of the 25th. I mention these facts of transportation to show the immense fatigue and suffering that this patient must have sustained before he reached his destination. Saw him about six o'clock A.M., found him suffering great agony; examined his wound. The ball had entered one line to the left and below the ensiform cartilage, passing through the abdominal cavity, and making its appearance under the skin just above the crest of the left ilium posteriorly, where it was excised at the field hospital. Pulse quick and exceedingly feeble, abdomen distended and tympanitic; took food and stimuli readily, and became much easier under the free use of opium. Patient was much emaciated, and countenance ghastly and indicative of greaf suffering. About noon saw him again; found him much more comfortable, wounds suppurating nicely and looked well; he expressed himself as expecting soon now to get well. About four o'clock P.M. was conversing with the nurse; apparently in good spirits, without very great pain; swallowed his medicine, etc., and in about five minutes afterward was in articulo mortis. The autopsy, which was made some hours after, showed the ball to have perforated the inferior curvature of the stomach, and strange as it may seem, although an orifice was made directly through the walls of the stomach large enough to admit two fingers, no inflammation or even congestion could be detected, except in the immediate locality of the wound, which was beginning to suppurate. . . . The pancrease was perforated at about its middle, but except in the immediate tract of the ball, gave evidence of no departure from its healthy standard; . . . General peritonitis had prevailed, and was undoubtedly the cause of death. In this case life was sustained for a period of fifteen days, notwithstanding the serious injury of a vital organ and the being subjected to the most unfavorable circumstances and depressing influences.[24]

During World War I only 5 pancreatic injuries were noted by the British Army among 965 casualties[13] and among American troops the incidence was 0.2 per cent among abdominal injuries.[32] Similarly, in the Spanish Civil War an incidence of 0.4 per cent among 970 abdominal injuries was noted.[16] In this period wounds of the pancreas remained almost universally fatal. Moynihan,[22] in World War I, observed only one patient who recovered and remained well.

Poole[26] summarized the experiences in the management of 62 casualties with pancreatic injuries from World War II; 2 per cent of 3,154 abdominal injuries. These represented penetrating injuries treated in the era of operative intervention. Great vessels were injured in 13, 5 being injuries of the inferior vena cava. Additional organs were injured in 61 of the 62 patients. Every patient was in shock when first seen. The mortality rate was 56 per cent (Table V). The diagnosis was established only at autopsy in 3 patients, the injury having been overlooked at laparotomy. Shock and hemorrhage were the causes of death of 26 patients (74 per cent), including 5 late deaths from

posttraumatic renal insufficiency, while 9 (24 per cent) died primarily from other specific complications of the associated injuries. Injury to the pancreas was the primary cause of death in only one patient, who died of pancreatitis. Of the patients with injuries to the great vessels, 11 died, including all 5 with vena caval injuries.

TABLE V. MILITARY EXPERIENCES WITH PENETRATING WOUNDS OF THE PANCREAS

| WAR | NUMBER OF PATIENTS | INCIDENCE (PER CENT OF ABDOMINAL INJURIES) | MORTALITY | |
|---|---|---|---|---|
| | | | PER CENT | NO. |
| American Civil War 1861-1865 | 5 | | 80 | 4 |
| World War I | | | | |
| British 1914-1918 | 5 | | 80 | 4 |
| American 1917-1918 | | 0.2 | | |
| Spanish Civil War 1936-1939 | 4 | 0.4 | | |
| World War II 1941-1945 | 62 | 2.0 | 56 | 35 |
| Korean Conflict 1952-1953 | 9 | 2.3 | 22 | 2 |

In the Korean conflict, advances in the treatment of shock and hemorrhage permitted further progress, the mortality from pancreatic injuries falling to 22 per cent (2 of 9 patients).[27]

During the past 10 years 20 articles have appeared in the English literature which deal specifically with pancreatic injuries in the civilian population. These reports summarize only 53 cases,[1-8, 10, 12, 15, 17, 18, 20, 21, 25, 29, 31, 33, 36] for only one series included more than 6 patients. It is noteworthy that all but one of these reports were concerned with pancreatic injury from blunt trauma. Matthewson[20] discussed briefly a small group of penetrating wounds as well as 9 patients with blunt trauma. His series is excluded from Table VI for lack of applicable data.

TABLE VI. COMPLICATIONS OF PANCREATIC INJURY FROM BLUNT TRAUMA COLLECTED FROM ENGLISH LITERATURE (1945-1954)

| NUMBER OF PATIENTS | NUMBER DEVELOPING PSEUDOCYST | NUMBER DEVELOPING FISTULA | MORTALITY |
|---|---|---|---|
| 36 | 12 (33%) | 13 (36%) | 3 (8%) |

Definitive data are available on 36 patients with blunt trauma reported during this period. The mortality was only 8 per cent but the incidence of pancreatic complications was quite high (Table VI). The low mortality is probably a reflection of the fact that the pancreas was the only organ injured in 31 of the 36 patients, but it may also reflect a selection of patients since most of them were presented as individual case reports.

The decrease in mortality following pancreatic wounds which has occurred in the past forty years is largely due to the practice of prompt surgical

intervention in abdominal wounds, plus utilization of the numerous surgical adjuncts which have become so important in the care of all surgical patients. One sees the same mortality pattern following this type of injury as that after injury to any other intra-abdominal viscus; namely, the mortality is directly proportional to the number of organs or major vessels injured. In our series the mortality resulting from the pancreatic wound per se was nil. All patients who died sustained injuries to 2 or more organs or major vessels in addition to the pancreatic injury. Consequently, mortality will be kept at a minimum when the patient is optimally prepared for surgery, shock is successfully combated, no injuries are overlooked, and mature judgment is exercised in the management of associated injuries at the time of operation.

With the exception of an occasional caudal amputation, it appears that little can be done to prevent the development of pancreatic complications, particularly fistula formation and cyst formation. The development of the latter complication is usually relatively late and is rarely of concern in the immediate postoperative period. However, pancreatic fistulas may become difficult problems. We were fortunate in that most of the fistulas in this series were minor, although, in one instance the daily output was initially as great as 1,350 ml. per twenty-four hours. Under such circumstances "sump" suction is employed to prevent skin excoriation, or pocketing of pancreatic juice, and to assure virtually complete collection of all drainage for measurement and analysis. The management of fluid and electrolyte balance must be meticulous. Although parasympathetic blocking agents cause a diminution in pancreatic secretion, they are of questionable value in the long-term management of difficult cases. Nutrition by mouth is encouraged as soon as it is tolerated, for the ease of fluid and electrolyte control, plus the adequate supply of calories which can be obtained only in this manner far outweighs any theoretical disadvantage of pancreatic stimulation. In an occasional patient, the collected pancreatic juice may be returned orally in order to maintain the body's economy. Our experience has been similar to that of others in that most pancreatic fistulas close spontaneously. Only one has drained for more than two months, and the drainage in this patient has been so slight that a major operative procedure to correct this disability has not been warranted.

## REFERENCES

1. Aldis, A. S.: Injuries to the Pancreas and Their Surgical Treatment (Hunterian Lecture), Brit. J. Surg. **33**: 323, 1946.
2. Barnbrook, D. H.: Impermanent Diabetes: Complication of Traumatic Pancreatitis, Canad. M. A. J. **67**: 143, 1952.
3. Becker, W. F.: Traumatic Pancreatitis, Am. Surgeon **20**: 525, 1954.
4. Catell, R. B., and Warren, K. W.: Surgery of the Pancreas, Philadelphia, 1953, W. B. Saunders Company.
5. Connolly, E. A., and Lempka, A. W.: Pseudocyst of the Pancreas, Am. J. Surg. **74**: 805, 1947.
6. Curr, J. F.: Complete Rupture of the Pancreas, Brit. J. Surg. **32**: 386, 1945.
7. DeMuth, W. E., Jr., and Rawson, A. J.: Pseudomonas Septicemia and Endocarditis; Report of Case, Am. J. M. Sc. **216**: 95, 1948.
8. Estes, W. L., Jr., Bowman, T. L., and Meilicke, F. F.: Nonpenetrating Abdominal Trauma with Special Reference to Lesions of Duodenum and Pancreas, Am. J. Surg. **83**: 434, 1952.
9. Fischer, H.: Injuries of the Pancreas, Am. J. Surg. **26**: 257, 1912.

10. Flavell, G.: Post-Traumatic Fistula of Pancreas, Successfully Treated by Surgery, Lancet **1:** 869, 1947.
11. Garre, C.: Totalen Querriss des Pankreas durch Naht geherlt, Beitr. klin. Chir. **46:** 233, 1905.
12. Hart, J. F., and Lisa, J. R.: Isolated Nonpenetrating Injuries of Pancreas; Ten Year Review of Literature and Report of Case, New York J. Med. **48:** 903, 1948.
13. History of the Great War Based on Official Documents, Vol. I, London, 1922, Medical Services Surgery of the War, His Majesty's Stationery Office.
14. Howard, J. M., Frawley, J. P., and Artz, C. P.: A Study of Plasma Amylase Activity in the Combat Casualty, Ann. Surg. **141:** 337, 1955.
15. Innerfield, I., and Ciancimino, F. E.: Acute Traumatic Pancreatitis Complicating Multiple Fractures, New York J. Med. **52:** 744, 1952.
16. Jolly, D. W.: Field Surgery in Total War, New York, 1941, Paul B. Hoeber, Inc.
17. Joseph, M.: The Pancreas and the Steering Wheel, West. J. Surg. **60:** 129, 1952.
18. Kipen, C. S.: Pancreatic Calculosis Following Trauma; Report of Case, SURGERY **27:** 914, 1950.
19. Kleberg: Arch. klin. Chir. **9:** 2, 1868. Quoted in ref. 24, p. 159.
20. Matthewson, C., Jr., and Halter, B. L.: Traumatic Pancreatitis With and Without Associated Injuries, Am. J. Surg. **83:** 409, 1952.
21. McHardy, G., Browne, D. C., and Welch, G.: Traumatic Rupture of Pancreas; Case Report, New Orleans M. & S. J. **99:** 511, 1947.
22. Moynihan, B. G. A.: Abdominal Operations, Philadelphia, 1926, W. B. Saunders Company.
23. Naffziger, H. C., and McCorkle, H. J.: Recognition and Management of Acute Trauma to the Pancreas, with Particular Reference to Use of Serum Amylase Test, Ann. Surg. **118:** 594, 1943.
24. Otis, G. A. (ed.): The Medical and Surgical History of the War of the Rebellion. Part II, Vol. II, Surgical History, Washington, D. C., 1876, Government Printing Office.
25. Phillips, S. K., and Seybold, W. D.: Traumatic Rupture of the Pancreas; Report of Case and Brief Review of Literature, Proc. Staff Meet., Mayo Clinic **23:** 254, 1948.
26. Poole, L. H.: Wounds of the Pancreas, Chapter XIX. Surgical History of World War II. To be Published. Washington, D. C., Office of the Surgeon General, Government Printing Office.
27. Sako, Y., Artz, C. P., Howard, J. M., Bronwell, A. W., and Inui, F. K.: A Survey of Evacuation, Resuscitation, and Mortality in a Forward Surgical Hospital, SURGERY **37:** 602, 1955.
28. Schmeiden, V., and Sebening, W.: Surgery of the Pancreas, Surg., Gynec. & Obst. **46:** 735, 1928.
29. Shallow, T. A., and Wagner, F. B.: Traumatic Pancreatitis, Ann. Surg. **125:** 66, 1947.
30. Stern, E. L.: Traumatic Injuries to the Pancreas, Am. J. Surg. **8:** 58, 1930.
31. Tabaka, F. B., Nigro, S. J., and Nora, E.: Traumatic Diaphragmatic Hernia Complicated by Acute Traumatic Pancreatitis, Illinois M. J. **101:** 269, 1952.
32. The Medical Department of the United States Army in the World War. Vol. XI, Part I, Washington, D. C., 1927, Government Printing Office.
33. Traquair, K.: Chylothorax Following Traumatic Pseudocyst of Pancreas, Brit. J. Surg. **33:** 297, 1946.
34. Travers, B.: Rupture of the Pancreas, Lancet **12:** 384, 1827.
35. von Mikulicz, J.: Surgery of the Pancreas, Ann. Surg. **38:** 1, 1903.
36. Wright, L. T., Prigot, A., and Hill, L. M.: Traumatic Subcutaneous Injuries to Pancreas, Am. J. Surg. **80:** 170, 1950.

# THE EFFECTS OF HYPOTHERMIA ON THE PHYSIOLOGY OF THE NERVOUS SYSTEM

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SINCE the introduction of hypothermia as a surgical adjunct, it has become increasingly apparent that much of the utility of this technique depends upon its effects on the physiology of the nervous system. Hypothermia is being currently employed to produce a generalized reduction in body metabolism which then permits an interruption of the circulation to vital centers for longer periods than can be tolerated at normothermic levels. Thus the arterial supply to the brain may be occluded for as long as twenty minutes at 20° C. and the flow to the spinal cord for ninety to one hundred eighty minutes at 23 to 26° C. without incurring the risk of producing a neurological deficit.[1, 2] Intricate cardiovascular and neurological surgery can then be accomplished which heretofore had been either extremely hazardous or impossible.[3-8] It has been assumed that total body oxygen consumption and cerebral oxygen consumption parallel each other during hypothermia, but direct measurements of cerebral functions have not been made. It is the purpose of this report to review the results of a series of experiments designed to evaluate the effects of temperature reduction on the nervous system and to correlate these findings with that information available from the literature.

It was first necessary to establish the effect of hypothermia on cerebral metabolism and vascular dynamics. A method was developed to measure cerebral blood flow in the dog which allowed continuous observations of flow throughout the experimental period.[9] As cerebral blood flow was measured, periodic blood samples were drawn for the determination of cerebral arterial and venous oxygen contents. The arterial blood source was the internal carotid artery, the venous source was the superior sagittal sinus. Cerebral oxygen consumption, the product of the cerebral blood flow and the arteriovenous oxygen difference, was then calculated. Systemic blood pressure was recorded continuously from a catheter threaded into the aorta through a femoral artery. Each animal was anesthetized with pentobarbital, 30 mg. per kilogram of body weight intravenously, intubated, and ventilated with 100 per cent oxygen by an automatic positive-negative respirator. Hypothermia was achieved by immersion to the shoulders in ice water. Temperatures were recorded from a thermistor inserted 200 mm. into the esophagus.

Received for publication Sept. 6, 1955.

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*Cerebral Blood Flow.*—The effect of hypothermia on the cerebral blood flow of 10 dogs is depicted in Fig. 1. Body temperature during the precooling control period was usually between 35° and 36° C. In order to facilitate comparative analysis of the data, values at 35° C., interpolated when necessary, were designated as 100 per cent at the control level. The blood flows of the individual animals, expressed as per cent of the flow observed at 35° C., were plotted against temperature. Each point in the scattergram represents the mean value of cerebral blood flow at that temperature level. Cerebral blood flow varied proportionately with changes in temperature. The average decrease in cerebral blood flow per degree decline of temperature between 35 and 25° C. was 6.7 per cent of the control level. At 25° C. cerebral blood flow was one-third of the precooling value.

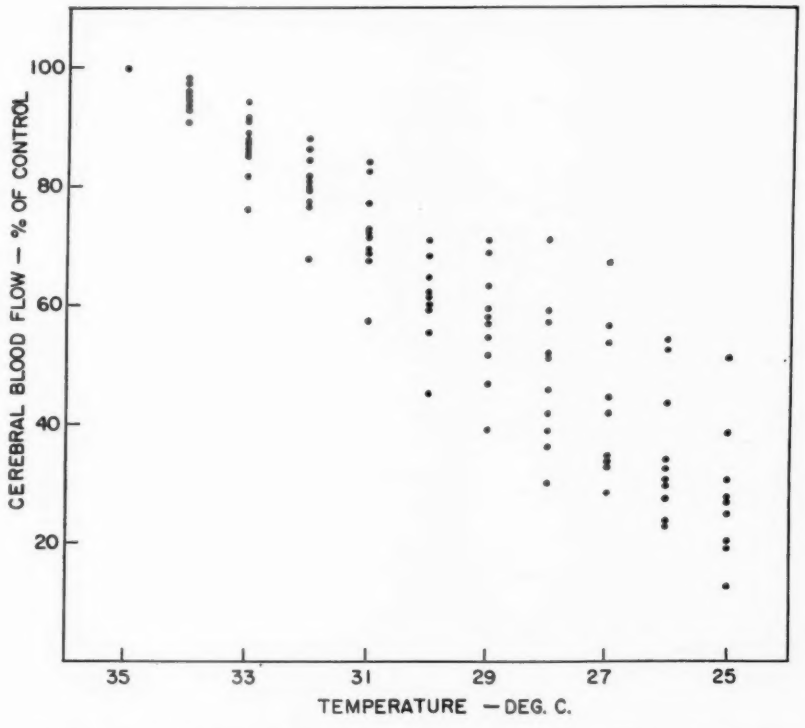


Fig. 1.—The cerebral blood flow of 10 dogs between 35° and 25° C.

*Blood Pressure and Cerebral Vascular Resistance.*—Systemic blood pressure maintained a similar relationship to temperature as did cerebral blood flow. The average decrease in blood pressure was 4.8 per cent of the control value per degree between 35 and 25° C. When the mean blood pressure and blood flow of a circulatory system are known, the vascular resistance may be calculated. Cerebral vascular resistance is the quotient of the mean blood pressure divided by the cerebral blood flow. The relationships of these three factors during hypothermia are illustrated in Fig. 2. Each function is expressed as the per cent of the control value observed at 35° C. and is plotted against temperature. As temperature was reduced, cerebral blood flow de-

creased in a linear fashion. Average mean blood pressure decreased in a similar but somewhat less constant manner. Average cerebral vascular resistance increased; however this function exhibited considerable variability. Although average systemic blood pressure showed a steady decline as temperature was reduced, individual determinations at each temperature level demonstrated large oscillations in contrast to cerebral blood flow which was relatively constant. Cerebral vascular resistance, therefore, must have changed considerably in order to maintain the constancy of blood flow in the face of a fluctuating blood pressure. Hence, it seems likely that cerebral vascular tone is actively regulated at all temperatures down to 25° C., probably as some function of the respiratory gas tensions in the brain.

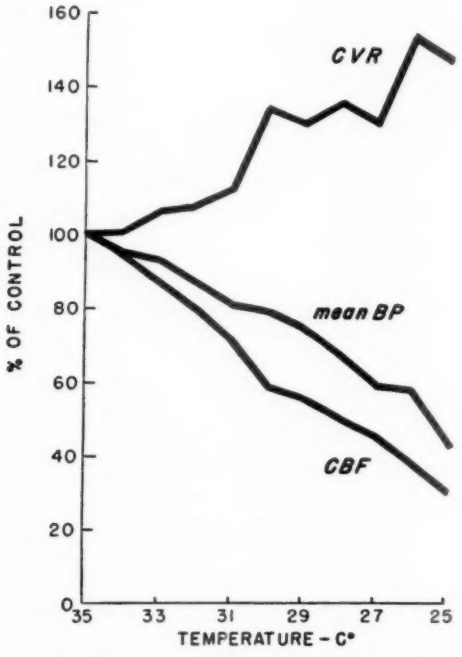


Fig. 2.—The relationships of cerebral blood flow, mean blood pressure, and cerebral vascular resistance during hypothermia.

*Cerebral Metabolism.*—As cerebral blood flow was recorded, simultaneous arterial and venous oxygen determinations were made and the cerebral oxygen consumption was calculated. Cerebral blood flow decreased as the temperature was reduced while the arteriovenous oxygen difference remained almost unchanged. Therefore, cerebral oxygen consumption must have decreased at the same rate as blood flow. In Fig. 3, the mean cerebral blood flow and oxygen uptake of 4 dogs are plotted with their control values adjusted to the same levels. Cerebral oxygen consumption and cerebral blood flow decreased at the same rate with decline in temperature so that at 25° C. both were one-third of the precooling level. Lougheed and Kahn[10] also found a progressive decrease in cerebral metabolic rate. In addition, these investigators determined serially the lactate-pyruvate ratio of cerebral arterial and venous blood.

The lactate-pyruvate ratio was used as an indicator of the absence or presence of hypoxia. When hypoxia occurs, the serum lactate concentration increases but the pyruvate level remains constant or decreases. No change in the ratio of serum lactate to pyruvate was observed during hypothermia. In vitro studies have also shown that brain slice oxygen consumption decreases with temperature reduction,[11] and exhaustive histologic studies have failed to demonstrate any evidence of cellular damage or loss.[10] Therefore, it is probable that hypoxia of brain tissue does not occur during hypothermia in this temperature range, so long as adequate respiratory and circulatory functions are maintained.

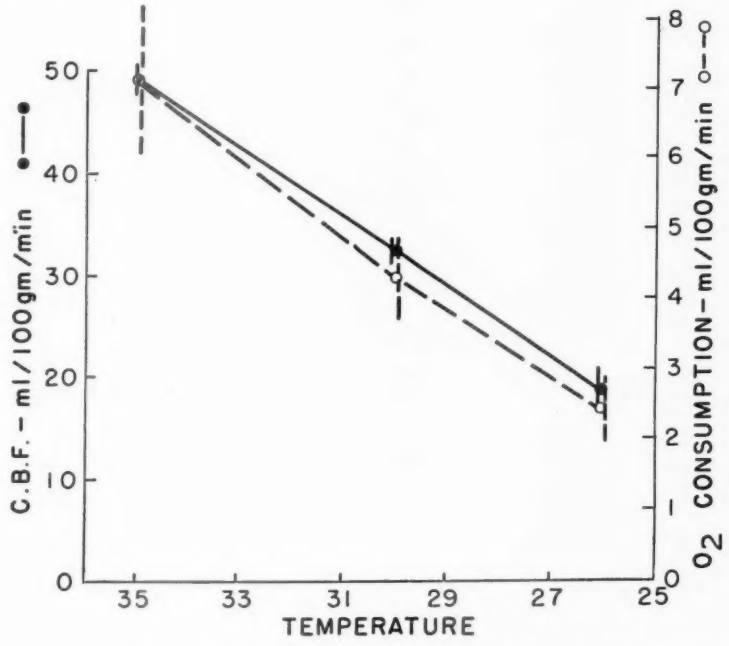


Fig. 3.—The solid circles joined by the solid lines represent the mean cerebral blood flow of 4 animals at 35°, 30°, and 26° C. The open circles joined by the broken lines represent the mean cerebral oxygen consumption of the same animals. The vertical lines represent the standard error of each mean. (From Am. J. Physiol. 179: 85, 1954.)

It was noted that the brain appeared smaller at 25° C. than at normothermic levels. Studies were conducted in an attempt to verify this observation and to quantitate the degree of change.[12] Brain volumes were determined by the method of White and his co-workers,[13] and intracranial pressure and venous pressure were measured simultaneously from catheters in the cisterna magna and jugular vein, respectively.

*Brain Volume.*—The brain volumes of 4 dogs were determined at 37° C. body temperature in order to establish control values. At this temperature the brain occupied 89 per cent of the cranial capacity of the dog, while the extracerebral space, meaning that intracranial space not occupied by brain, was 11 per cent of the total. Nine animals were subjected to hypothermia of 25° C. and their brain volumes were estimated. The per cent change of

brain volume and the per cent change of the extracerebral space were calculated. These are presented in Table I. Assuming that the relative sizes of the brains of the experimental dogs prior to the induction of hypothermia were equal to those of the controls, then at 25° C. their brain volumes must have decreased 4.1 per cent. This is equivalent to 3 ml. in the average 10 kg. dog. If a similar change were to occur in man, it would amount to 55 ml.

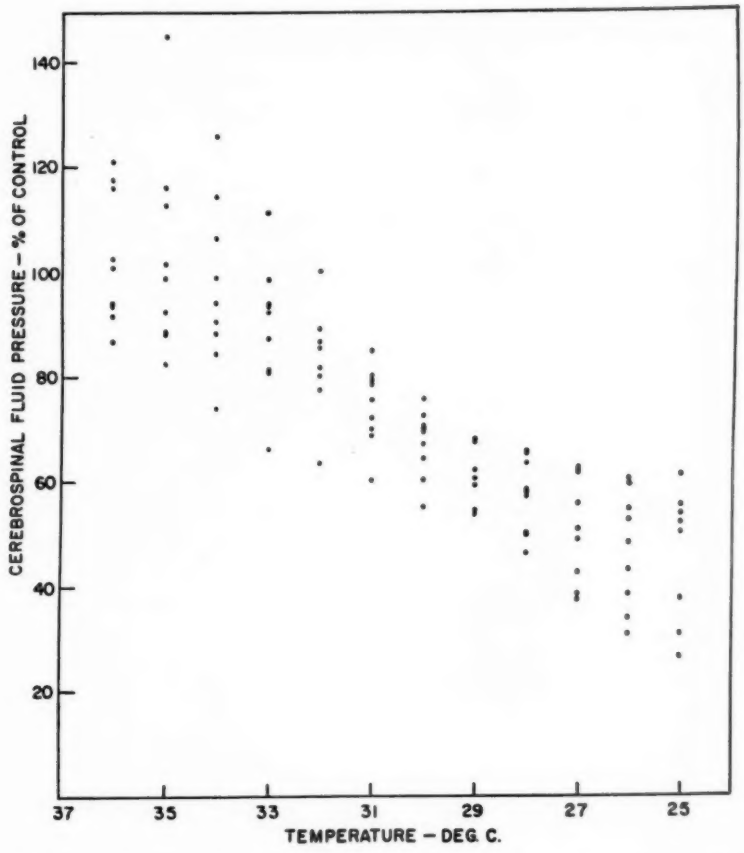


Fig. 4.—The cerebrospinal fluid pressures of 9 dogs between 37° and 25° C.

in the average adult. Such a change, coupled with the resultant 31.8 per cent increase in extracerebral space assumes considerable practical significance when dealing with certain neurologic operative conditions or pathologic processes.[7, 8]

*Cerebrospinal Fluid Pressure.*—Observations were made on 9 dogs (Fig. 4). The cerebrospinal fluid pressures of each animal, expressed as per cent of the pressure observed at 37° C. are plotted against temperature. There was an inconstant initial response to the application of cold. In 5 animals, the cerebrospinal fluid pressure increased; in 4 animals a decline was observed. Thereafter, there was a progressive decrease in cerebrospinal fluid pressure

with reduction of temperature in all animals. The estimated decrease of cerebrospinal fluid pressure per degree decline of temperature between 37° and 25° C. was 5.6 per cent of the control value.

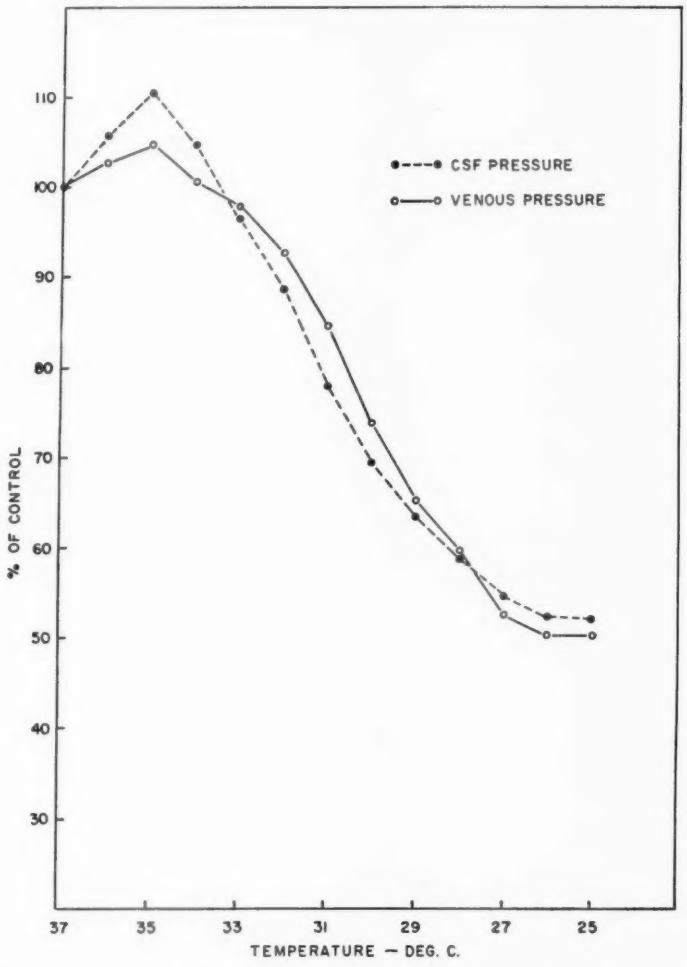


Fig. 5.—The average cerebrospinal fluid pressure and venous pressure during hypothermia. (From Am. J. Physiol. 183: 19, 1955.)

*Venous Pressure.*—The effect of hypothermia on venous pressure is shown in Fig. 5. The average decrease in venous pressure was 5.4 per cent of the control value per degree between 37° and 25° C. This study raised two interesting questions: what is the effect of shivering on venous and cerebrospinal fluid pressure and what is the effect of respiration on both these functions during hypothermia?

Bigelow and his co-workers[14] have demonstrated that shivering raises venous pressure. This study corroborated that finding and made the additional observation that cerebrospinal fluid pressure becomes elevated as well. The initial increases of both venous and cerebrospinal fluid pressures in some of the animals in this series coincided directly with the appearance of shivering.

When shivering did not occur or when it was eliminated by supplementary doses of pentobarbital, no increase in either pressure was noted. This indicates the need for proper and adequate anesthesia during the induction of hypothermia. It must be recognized that shivering may be occult and may be detectable only by specialized techniques such as electromyography or oxygen consumption measurements.

When animals are allowed to breathe spontaneously, the application of cold is accompanied by a slight fall in venous pressure which thereafter remains stationary as long as respirations are adequate. However, respirations become depressed as the temperature decreases and artificial respiration becomes necessary. When artificial respiration is instituted, venous pressure gradually increases, often to alarming heights. Dogs with high venous pressures usually exhibit severe cardiac arrythmias, such as ventricular fibrillation, from which they seldom recover. Reduction of venous pressure by venesection restores regular heart activity in the majority of instances.[14]

TABLE I. CHANGES IN BRAIN VOLUME AND CHANGES IN EXTRACEREBRAL SPACE IN NINE HYPOTHERMIC DOGS (25° C.)

| DOG NO. | CHANGE IN BRAIN VOLUME (PER CENT) | CHANGE IN EXTRACEREBRAL SPACE (PER CENT) |
|---|---|---|
| 1 | -8.5 | +68.9 |
| 2 | -3.3 | +26.3 |
| 3 | -4.0 | +32.2 |
| 4 | -2.9 | +23.8 |
| 5 | -4.8 | +36.2 |
| 6 | -3.5 | +28.6 |
| 7 | -5.3 | +42.4 |
| 8 | -3.3 | +27.0 |
| 9 | -1.3 | + 9.9 |
| Means | -4.1 | +31.8 |

When animals are hyperventilated by a positive pressure respirator with a high mean mask pressure, no change in venous pressure is observed and a lesser incidence of cardiac arrythmias is found.[15] In the present study hyperventilation was also utilized; however, a respirator was used which produced a negative as well as a positive phase. Hyperventilation was employed to avert the development of the acidosis commonly associated with hypothermia in animals not so controlled.[15-17] A negative phase was introduced into the respiratory cycle with the hope that venous pressure might be better regulated. A negative phase at normal body temperature decreases venous pressure, increases venous return, and augments cardiac efficiency.[18] The results of this investigation suggest that a negative phase in the respiratory cycle has a continuous beneficial effect during hypothermia. There was a progressive decrease in venous pressure and cerebrospinal fluid pressure; ventricular fibrillation was not observed.

To recapitulate, this series of experiments indicates that during hypothermia there is a decreased cerebral blood flow, a corresponding decline in

cerebral metabolism, a compensated hypotension, a decrease in brain volume, and a diminution of intracranial pressure. All of these are reversible on rewarming, and all are apparently without residual ill effects.

*Electrical and Reflex Activity.*—Several other pertinent observations of the effect of temperature reduction on nerve physiology have been made. Chatfield[19] reported a steady depression of peripheral nerve conduction until a level of 9° C. was reached, below which no potentials could be recorded. Noell and Brill studied the relationship between temperature and times of conduction and excitation along the visual pathway. The responses of the retina, optic nerve, and arcs with one and two synaptic delays were plotted and compared. All progressively decreased with temperature and at the same rate.[20] The electroencephalograms of several species have been investigated. All showed a steady reduction in brain wave amplitude and frequency as temperature was lowered.[21-24] Spontaneous cortical electrical activity disappeared between 17 and 21° C. However, between 17 and 9° C. evoked potentials could still be recorded. Below 9° C., electrical silence prevailed.[21]

Callaghan and his co-workers have studied the effect of hypothermia on training and behavior.[24] A group of trained monkeys were cooled to a body temperature of 20° C. on two or three separate occasions. After rewarming there was no demonstrable impairment in the animals' behavior or their ability to solve test problems. This is interpreted as evidence that hypothermia does not affect adversely those higher cerebral processes which are concerned with these functions. Likewise, no neurological aberrations following hypothermia have been reported in man.

Finally, Fay and Smith[25] described the responses of patients subjected to hypothermia for the treatment of cancer. They noted an initial hyperactivity of deep tendon reflexes accompanied by drowsiness, slowing of activity, thickening of speech, incoordination of fine finger movements, and the appearance of shivering. As cooling continued, the reflexes became progressively less active and below 25° C. they were unobtainable. At this point the patients were unable to speak and they were "cold anesthetized."

The influence of temperature on the nervous system is remarkably consistent. All functions studied to date have shown a progressive depression of activity with the lowering of temperature thereby affording advantages which could become important factors in the investigation and treatment of abnormal states of the nervous system. Reports have already begun to appear which indicate that hypothermia is of value in the therapeutic approach to certain neuropathological processes, particularly those involving the vascular components of the brain.[26, 27] The potential seems great and the possibilities are infinite, which should make hypothermia an increasingly more frequent subject for consideration in basic as well as clinical research.

## SUMMARY

During hypothermia there is (1) a decrease in cerebral blood flow, (2) a corresponding decline in cerebral metabolism, (3) a compensated hypotension,

(4) a decrease in brain volume, (5) a diminution of intracranial pressure, and (6) a depression of electrical and reflex activity.

## REFERENCES


1. Bigelow, W. E., Mustard, E. T., and Evans, J. G.: Some Physiologic Concepts of Hypothermia and Their Applications to Cardiac Surgery, J. Thoracic Surg. **28**: 463-480, 1954.
2. Owens, J. C., Prevedel, A. E., and Swan, H.: Prolonged Experimental Occlusion of the Thoracic Aorta During Hypothermia, Arch. Surg. **70**: 95-97, 1955.
3. Bigelow, W. E., Callaghan, J. C., and Hopps, J. A.: General Hypothermia for Experimental Intracardiac Surgery, Ann. Surg. **132**: 531-537, 1950.
4. Bailey, C. P., Cookson, B. A., Downing, D. F., and Neptune, W. B.: Cardiac Surgery Under Hypothermia, J. Thoracic Surg. **27**: 73-95, 1954.
5. Swan, H., Zeavin, I., Blount, S. G., Jr., and Virtue, R. W.: Surgery Under Direct Vision in the Open Heart During Hypothermia. J. A. M. A. **153**: 1081-1085, 1954.
6. Lewis, F. J., Varco, R. L., and Taufic, M.: Repair of Actual Septal Defects in Man Under Direct Vision With the Aid of Hypothermia, SURGERY **36**: 538-556, 1954.
7. Botterell, H. E., and Lougheed, W. M.: A Discussion of the Surgical Treatment of Sixteen Cases of Intracranial Aneurysm Using Hypothermia, Proc. Harvey Cushing Soc. (Quebec), May 16-18, 1955.
8. Rosomoff, H. L.: The Effects of Hypothermia on Cerebral Physiology: Applications in Neurological Surgery, Proc. Harvey Cushing Soc. (Quebec), May 16-18, 1955.
9. Rosomoff, H. L., and Holaday, D. A.: Cerebral Blood Flow and Cerebral Oxygen Consumption During Hypothermia, Ann. J. Physiol. **179**: 85-88, 1954.
10. Lougheed, W. M., and Kahn, D. S.: Circumvention of Anoxia During Arrest of Cerebral Circulation for Intracranial Surgery, J. Neurosurg. **12**: 226-239, 1955.
11. Field, J., 2nd., Fuhrman, F. A., and Martin, A. W.: Effects of Temperature on the Oxygen Consumption of Brain Tissue, J. Neurophysiol. **7**: 117-126, 1944.
12. Rosomoff, H. L., and Gilbert, R.: Brain Volume and Cerebrospinal Fluid Pressure During Hypothermia, Am. J. Physiol. **183**: 19-22, 1955.
13. White, J. C., Verlot, M., Selverstone, B., and Beecher, H. K.: Changes in Brain Volume During Anesthesia; Effects of Anoxia and Hypercapnia, Arch. Surg. **44**: 1-21, 1942.
14. Bigelow, W. E., Lindsay, W. K., and Greenwood, W. F.: Hypothermia. Its Possible Role in Cardiac Surgery. An Investigation of Factors Governing Survival in Dogs at Low Body Temperatures. Ann. Surg. **132**: 849-866, 1950.
15. Deterling, R. A., Nelson, E., Bhonslay, S., Howland, W.: Study of Basic Physiologic Changes Associated With Hypothermia, Arch. Surg. **70**: 87-94, 1955.
16. Osborn, J. J.: Experimental Hypothermia: Respiratory and Blood pH Changes in Relation to Cardiac Function, Am. J. Physiol. **175**: 389-394, 1953.
17. Fleming, R.: Acid-base Balance of the Blood in Dogs at Reduced Body Temperature, Arch. Surg. **68**: 145-152, 1954.
18. Hubay, C. A., Waltz, R. C., Brecher, G. A., Praglin, J., and Hingson, R. A.: Circulatory Dynamics of Venous Return During Positive-negative Pressure Respiration. Anesthesiology **15**: 445-461, 1954.
19. Chatfield, P. O.: Effects of Cooling on Nerve Conduction in a Hibernator and Nonhibernator, Am. J. Physiol. **155**: 179-185, 1948.
20. Noell, W. K., and Brill, S. A.: Effects of Hypothermia on Brain Activity, Air Force School of Aviation Medicine, Report #1, Proj. #21-1202-0003, p. 1-33, 1953.
21. Chatfield, P. O., Lyman, C. P., and Purpura, D. P.: The Effects of Temperature on the Spontaneous and Induced Electrical Activity in the Cerebral Cortex of the Golden Hamster, Electroencephalog. & Clin. Neurophysiol. **3**: 225-230, 1951.
22. Ten Cate, J.: The Influence of Body Temperature on the Electroencephalogram of the Rat, Electroencephalog. & Clin. Neurophysiol. **1**: 231-235, 1949.
23. Libet, B., Fazekas, J. F., Meirowsky, A. M., Campbell, E. H., and Himwich, H. E.: Control of Electrical and Oxidative Activity of Brain by Temperature, Am. J. Physiol. **129**: 404-405, 1940.
24. Callaghan, J. C., McQueen, D. A., Scott, J. W., and Begelow, W. G.: Cerebral Effects of Experimental Hypothermia, Arch. Surg. **68**: 208-215, 1954.
25. Fay, T., and Smith, G. W.: Observations of Reflex Responses During Prolonged Periods of Human Refrigeration, Arch. Neurol. & Psychiat. **45**: 215-222, 1941.
26. Lougheed, W. M., Sweet, W. H., White, J. C., and Webster, W. R.: The Use of Hypothermia in Surgical Treatment of Cerebral Vascular Lesions. A Preliminary Report, J. Neurosurg. **12**: 240-255, 1955.
27. Rosomoff, H. L.: Occlusion of the Middle Cerebral Artery Under Hypothermia, Fed. Proc. **14**: 125, 1955.

# SURVIVAL OF CORTISONE- AND CORTICOTROPIN-TREATED RATS DURING EXPOSURE TO COLD

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COLD stress constitutes an important factor in everyday life but many of the metabolic changes associated with low environmental temperature are poorly understood. It is possible that the adrenal cortex exerts a prominent role in protection against cold but the mechanism is complicated. The observation that the administration of cortine to adrenalectomized rats enables them to maintain their body temperature almost as well as that of normal rats (Hartman and Brownell[4]) was suggestive that a cortical hormone plays a role in heat generation. However, the later work of Horwath and associates[6, 7] indicated that rats deprived of their adrenals showed very little or no increase in susceptibility to cold but perhaps a slight decrease in basal heat production.[10] The work of Selye,[12] which is in agreement with that of Horwath indicates that, while the adrenals are not indispensable in cold, perhaps the thyroid is. Tysolwitz and co-workers,[15] and Leblond and associate[9] emphasized the importance of the pituitary-adrenal-thyroid interrelationship in resistance to cold. Later investigations of Fredrickson, Thorn and associate[2] had demonstrated that exogenous cortisone administration, conducted on euthyroid human beings, produced suppression of thyroid function as measured by $I^{131}$ methods.[14, 16] No answer was given as to the mechanism for such suppression. Pashkis[11, 13] believed that the inhibition is a direct action of cortisone on the thyroid gland while Hill[5] predicted suppression of pituitary thyrotropic hormone production. According to Engel[1] the metabolic effects of adrenal cortical hormone overdosage and stress may in reality be induced by stimuli other than those we ordinarily ascribe to the adrenal cortical hormone which, in his opinion, simply facilitates these reactions. Or according to Ingle's[8] permissive action theory, the stress sets up a complex chain reaction involving more than one hormone. Leblond and Gross[9] found that when total thyroidectomy was performed in rats just before exposure to cold, the survival time was considerably prolonged. It was fourteen and seven-tenths days on the average, while the controls died in an average of three and three-tenths days. Not mentioned in their conclusions, but perhaps of some importance, is the thought that the decreased circulating thyroid hormone level in the first group may have permitted an increased adrenal activity and perhaps a better heat preservation during the cold stress. Goldenberg, Hayes, and co-workers[3] postulated that the effects formerly thought to be solely adrenocortical in origin are the results of the thyroid-adrenocortical interrelationship. Thus, upon stress there is first an increased thyroid activity. Then the adrenocortex antagonizes the thyroid and restores the homostasis.

Received for publication Sept. 6, 1955.

TABLE I

| GROUP | EXPERIMENT NUMBER | AGENT | TREATMENT SCHEDULE | SURVIVED | | DIED | | TOTAL | | MORTALITY (PER CENT) | CHI SQ. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | NO. | M. W. GM.‡ | NO. | M. W. GM. | NO. | M. W. GM. | | |
| I, A | 1 | ACTH | 1 u./r.† divided in 2 doses during exposure | 7 | 190.28 | 18 | 188.83 | 25 | 189.24 | 72.0 | |
| | | 0.9 per cent NaCl | 0.2 ml. divided in 2 doses | 11 | 188.00 | 14 | 191.07 | 25 | 189.72 | 56.0 | 0.14 |
| I, A | 2 | Cortisone | 5 mg./r.* 24 hours pre-exposure | 10 | 191.70 | 15 | 189.50 | 25 | 190.40 | 60.0 | |
| | | 0.9 per cent NaCl | 0.1 ml./r. 24 hours pre-exposure | 6 | 188.66 | 19 | 186.68 | 25 | 187.10 | 76.0 | 0.15 |
| I, A | 3 | Cortisone | 2.5 mg./r. for 3 days | 9 | 189.68 | 16 | 192.37 | 25 | 191.28 | 64.0 | |
| | | 0.9 per cent NaCl | 0.1 ml./r. for 3 days | 10 | 189.30 | 15 | 183.66 | 25 | 185.92 | 60.0 | 0.08 |

*mg./r.: milligram per rat.
†u./r.: unit per rat.
‡M. W. Gm.: mean weight in grams.

In the literature there is no direct evidence that administration of adrenal cortical hormones influences the tolerance to low temperatures. Our investigation was designed to study the effects of cortisone and corticotropin on the sum of the metabolic processes—the survival rates in a statistically significant number of rats subjected to cold under various controlled conditions of exercise and rest and adrenocortical stimulation and depletion.

The experiments were divided into four main groups:

*Group I.* Short term, one to three days pretreatment with cortisone or corticotropin
A, 150 anesthetized animals.
B, 120 unanesthetized animals

*Group II.* Long term, ten to fourteen days pretreatment with cortisone, 230 animals.

The animals of Groups I and II were exposed to cold in a resting state.

*Group III.* Short term, one to three days pretreatment with cortisone or corticotropin, 96 animals.

*Group IV.* Long term, ten to fourteen days pretreatment with cortisone, 144 animals.

The animals of Groups III and IV were simultaneously exposed to cold and exercise.

Healthy Holtzman-strain female rats of approximately the same age and weight were kept at fairly constant room temperature of 25° C. at all times. Food, consisting of commercial fox chow and drinking water, was offered ad libitum. Before an experiment was started, each rat was weighed and identified by notching the ears. Each rat from the experimental group was matched with one from the control group, thus insuring a comparable weight distribution. The difference of the mean weights between the animals of the experimental and of the control group was never greater than ± 4 Gm.

*Group I, A.*—150 rats, treated one to three days with cortisone or corticotropin before exposure to cold. Exposure time one hour (Table I).

All rats anesthetized with pentobarbital, 30 mg. per kilogram given intraperitoneally immediately prior to exposure to cold.

The anesthetized animals were placed in a specially constructed box which was then moved to the cold room. Each animal occupied an individual compartment measuring 7.5 by 9 by 19 cm. The floor and the ceiling were constructed of ½-inch wire mesh to allow free convection of air and unobstructed vertical radiation. The 1-inch wood walls prevented radiation of heat from the other animals in nearby compartments. The temperature of the cold room was maintained at −9° C. The humidity and air circulation were constantly controlled.

In Experiment 1, corticotropin was the agent used to induce increased cortical activity. Each rat was given 0.5 unit of ACTH intraperitoneally immediately preceding the exposure to cold. The same dose was then repeated after one-half hour of exposure to cold. The control rats in this experiment

received 0.1 ml. of saline solution intraperitoneally at the same time the experimental animals were given the ACTH. After one hour of exposure to cold in the ACTH treated group of 25 rats, there were 18 deaths or a 72 per cent mortality as compared to the 25 control animals in which there were fourteen deaths or a 56 per cent mortality. This represents an insignificant increase in death rate in the ACTH treated rats.

The rats in Experiment 2 were prepared by the administration of cortisone acetate given intramuscularly in a dose of 5 mg. per rat as a single injection twenty-four hours before the exposure to cold. The 25 control rats received 0.1 ml. of 0.9 per cent saline solution intramuscularly on the same day as the experimental animals received the cortisone. After one hour of exposure to cold there were 15 deaths in the cortisone-treated group, or a mortality of 60 per cent. In the control group of 25 rats not treated with cortisone there were 19 deaths or 76 per cent mortality. These figures represent an insignificant decrease in mortality in the cortisone-treated animals and are quite similar to the results of Experiments 1 and 3.

In Experiment 3, essentially the same procedure was employed as in Experiment 2, except that cortisone acetate was given intramuscularly in a dose of 2.5 mg. per rat per day on three consecutive days. The last dose was administered one hour prior to exposure to cold. The control animals received 0.1 ml. of saline solution intramuscularly on corresponding days. In the experimental group, the number of dead animals after exposure to cold for one hour was 16 or a mortality of 64 per cent. In the 25 control animals, the corresponding figures were 15 dead animals or a mortality of 60 per cent. The mortality in both groups was essentially equal.

On the anesthetized animals in Experiments 1, 2, and 3 the rectal temperatures were recorded at five-minute intervals. Fig. 1 indicates that there was a gradual decrease of the temperature during the one hour of exposure to cold. The decrease in temperatures followed a straight line. The mean rectal temperature at the beginning of the experiment in the 12 cortisone-treated rats was + 32.5° C. and in the twelve controls it was + 33.3° C. The same picture prevailed during the whole time of exposure. At the end of the experiment (at sixty minutes) the mean rectal temperature of the cortisone-treated group was plus 20.5° C. whereas that of the control group was 22.0° C. It appears that the cortisone-treated group had a lower baseline in rectal temperatures. The fact that more animals (5 rats) died in the cortisone group than in the control group (3 rats) may account for the consistently lower mean rectal temperatures in the control group. To illustrate the contention that dead animals lose their body temperature more rapidly than anesthetized animals of equal size and under equal conditions, continuous rectal temperatures were taken of a rat killed immediately before exposure to cold. The curve is illustrated in Fig. 2. Rectal temperature curves of the cortisone-treated animals showed a widespread distribution (Fig. 2). The same picture was noted in the control group. The number of animals was too small to allow any conclusion about the difference in heat preservation between these two groups.

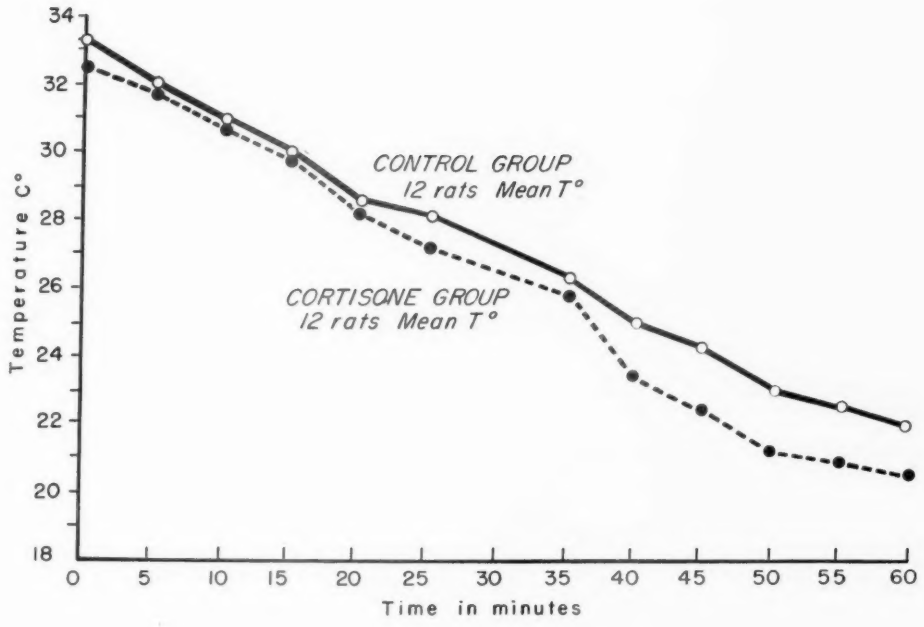
CONTROL GROUP
12 rats Mean T°
CORTISONE GROUP
12 rats Mean T°
Temperature C°
Time in minutes

Fig. 1.

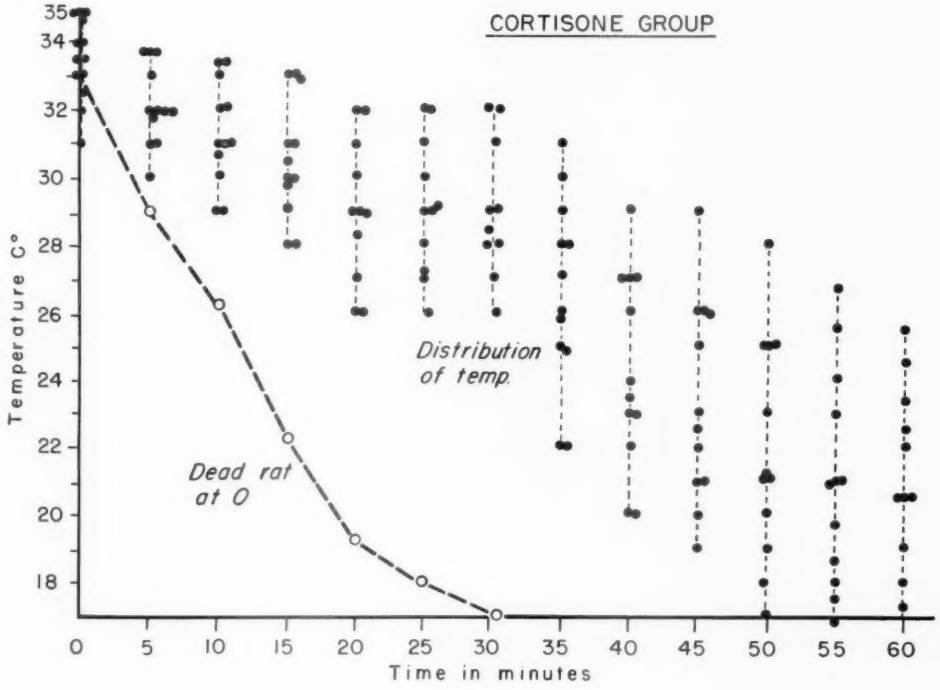
CORTISONE GROUP
Distribution of temp.
Dead rat at 0
Temperature C°
Time in minutes

Fig. 2.

TABLE II

| GROUP | NUMBER EXPERIMENT | AGENT | TREATMENT SCHEDULE | SURVIVED NO. | SURVIVED M. W. GM. | DIED NO. | DIED M. W. GM. | TOTAL NO. | TOTAL M. W. GM. | MORTALITY (PER CENT) | CHI SQ. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| I, B | 4 | Cortisone | 2.5 mg./r. for 3 days | 14 | 173.78 | 21 | 178.42 | 35 | 176.57 | 60.0 | |
| | | 0.9 per cent NaCl | 0.1 ml./r. for 3 days | 21 | 180.00 | 14 | 191.42 | 35 | 184.57 | 40.0 | 2.79 |
| I, B | 5 | ACTH | 0.5 u./r. in 4 doses over 2 days | 15 | 184.9 | 10 | 183.70 | 25 | 185.70 | 40.0 | |
| | | 0.9 per cent NaCl | 0.1 ml./r. in 4 doses over 2 days | 15 | 178.70 | 10 | 179.00 | 25 | 178.50 | 40.0 | 0.00 |

TABLE III

| GROUP | EXPERIMENT NUMBER | AGENT | TREATMENT SCHEDULE | SURVIVED NO. | SURVIVED M. W. GM. | DIED NO. | DIED M. W. GM. | TOTAL NO. | TOTAL M. W. GM. | MORTALITY (PER CENT) | CHI SQ. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| II | 6 | Cortisone | 2.5 mg./r. 14 days, 4-day pause | 31 | 207.64 | 9 | 215.66 | 40 | 209.45 | 22.5 | |
| | | 0.9 per cent NaCl | 0.1 ml./r. 14 days, 4-day pause | 27 | 220.66 | 13 | 213.53 | 40 | 218.35 | 32.5 | 0.61 |
| II | 7 | Cortisone | 2.5 mg./r. 2 days, 5-day pause, 3 days | 57 | 188.94 | 18 | 186.50 | 75 | 188.36 | 24.0 | |
| | | 0.9 per cent NaCl | 0.1 ml./r. 2 days, 5-day pause, 3 days | 16 | 203.18 | 59 | 201.00 | 75 | 202.80 | 78.7 | 28.38 |

*Group I, B.*—120 rats, treated two to three days with cortisone or corticotropin before exposure. No anesthesia was given. Exposure time twenty-four hours (Table II).

The pretreatment in Experiment 4 consisted of cortisone acetate intramuscularly in a dose of 2.5 mg. per rat per day for three consecutive days, the last dose of which was given one hour prior to exposure to cold. Control rats were treated similarly, but instead of cortisone they were given 0.1 ml. of saline solution intramuscularly. This experiment contained 70 rats divided into equal groups, one of which was the experimental group whereas the other represented the controls. The period of exposure had to be increased to twenty-four hours to obtain the approximate $LD_{50}$ in the control group. The animals were fasting during the entire period of exposure. The result was 60 per cent mortality or 21 deaths in the experimental group of 35 rats. In the control group of 35 rats there was an insignificantly smaller mortality of 40 per cent, or 14 deaths.

In Experiment 5, ACTH was used in a dose of 0.5 unit per rat twice daily, starting twenty-four hours before exposure and continuing through the twenty-four hours of the cold exposure; this represented a total dose of 4 units per rat for the forty-eight-hour period. The control group in this experiment was given 0.1 ml. of saline solution intramuscularly on a similar schedule. The result was that the 25 experimental rats had a 40 per cent mortality or 10 deaths. In the control group of 25 rats, the figures were the same. In this experiment, corticotropin did not exert any influence on the tolerance to cold.

*Group II.*—230 rats, treated with cortisone for 10 to 14 days before exposure to cold. Exposure time twenty-four hours (Table III).

Experiment 6 was designed to study the effect of adrenal suppression on tolerance to cold. Therefore, cortisone acetate was given in a dose of 2.5 mg. per rat per day to the 40 experimental animals for 14 consecutive days. A four-day period was allowed to elapse between the last dose of cortisone and the exposure to cold. The 40 control rats received 0.1 ml. of saline solution intramuscularly in the same manner as their respective experimental animals were given the cortisone. After twenty-four-hour exposure to cold there were 9 deaths or a mortality of 22.5 per cent in a group of 40 cortisone-treated rats. In the control group of forty rats without the cortisone pretreatment there were 13 deaths, or a 32.5 per cent mortality. These figures indicate an insignificant decrease in mortality rate for the adrenal-suppressed group and, therefore, no effect would be ascribed to this type of cortisone pretreatment.

Experiment 7 was conducted on 150 rats prepared by prolonged intermittent cortisone administration before exposure to cold. Cortisone was given in doses of 2.5 mg. per rat per day to the 75 experimental animals on two consecutive days, but no cortisone was administered for the next five days. The cortisone treatment was then resumed for the next three days, which was immediately followed by cold exposure. The last dose of cortisone was given one hour before the rats were placed in the cold room. The 75 control rats received 0.1 ml. of saline solution per rat per day, given intramuscularly

on corresponding days. The intermittent cortisone administration schedule was discovered incidentally during one of the numerous preliminary experiments. It was found to be highly effective in protecting the treated animals against low temperatures in every instance during these earlier experiments. The intermittent cortisone administration schedule accordingly was adapted and used empirically in the present experiments even though the explanation for its mode of action was lacking. After twenty-four-hour exposure to cold the following values were obtained. In the group of 75 cortisone-treated rats, there were eighteen deaths or a mortality of 24 per cent. The control group of 75 rats had 59 deaths which increased the mortality to 78.7 per cent. The statistical analysis revealed that this represents a highly significant figure. Rats were protected against low environmental temperatures if cortisone was administered according to this intermittent schedule. The mortality of the cortisone-treated group was lowered to one-third of that of the control animals.

The unanesthetized rats in the preceding experiments of Group I, *B* and Group II were not restricted from motion in the small individual compartments during the twenty-four-hour exposure to cold. Invariably in the first hour of cold exposure the animals showed an increased activity by walking and examining the interior of the cage, but after the second hour, the rats attained a crouching position with the tail and legs drawn close to the body, sitting motionless until the end of the experiment. The only noticeable activity was a generalized shivering. In Group I, *A* in which general anesthesia was employed, and hence shivering prevented, the rats were at absolute rest during the one-hour exposure to cold.

### COLD AND EXERCISE

The second part of this investigation deals with rats prepared in a similar manner to the preceding groups but subjected to cold and moderate exercise simultaneously. A slowly rotating type of exerciser was used, consisting of a motor-driven drum with six compartments, each of which comfortably accommodated four rats. The drum was set at a constant speed of one full revolution per fifty eight and eight-tenths seconds. The perimeter of the drum was 148.6 cm., thus the speed of any point of the perimeter of the drum was 91 meters per hour. To maintain their stance, the rats were forced to walk on the screen-covered floor at a constant speed which equaled that of the drum (or 91 meters per hour). The continuous walking by the animals was maintained remarkably well for the entire period of the cold exposure. Only the dead or dying animals were passively rolled around the drum. The time of cold exposure which was necessary to produce death in approximately 50 per cent of the animals ($LD_{50}$) varied from six to eight hours, and the distance a rat traveled was 550 to 750 meters. After completion of the experiment, the rats were removed from the exerciser and transferred back to regular cages at + 25° C. room temperature. The condition of some of the animals was critical at the completion of the experiment; some survived and some died. We arbitrarily decided upon an observation period of twelve hours, after which time the final mortality was recorded.

*Group III.*—96 rats, treated one to three days with cortisone or corticotropin before or during exposure to cold and exercise (Table IV).

The animals for Experiment 8 were prepared by cortisone administered for a short period; the drug was given intramuscularly in a dose of 2.5 mg. to each of the 24 experimental rats daily for three consecutive days. The last dose was given one hour prior to exposure to cold. The twenty-four control animals received 0.1 ml. of saline solution intramuscularly on the same days as the experimental group received cortisone. After exposure to cold for seven hours in the cortisone-pretreated group of 24 animals, this resulted in three deaths which equals 12.5 per cent mortality. The control group of twenty-four animals had seven deaths or a mortality of 29.2 per cent. These figures were statistically insignificant and no protection could be ascribed to short-term pretreatment with cortisone on rats during exposure to cold and exercise. The same results were obtained in Group I, *B* which indicated that short-term cortisone pretreatment did not increase the tolerance to cold in rats either at rest or during moderate exercise.

In Experiment 9, the adrenal activity was altered by exogenous corticotropin administration. ACTH was given intramuscularly as a dose of 2 units per rat one hour before the exposure to cold and again 2 units per rat for four hours after beginning the exercise. The control animals received 0.1 ml. of saline solution intramuscularly at corresponding intervals. After seven hours of exposure in the ACTH-treated group of 24 rats, there were 12 deaths or a 50 per cent mortality. In the 24 control rats the death rate was 11 rats, corresponding to a 45.8 per cent mortality. Again these figures represent an insignificant difference in the mortality rate between the two groups. One can conclude that ACTH in the given dosage did not exert any influence on the rats' tolerance to cold during exercise.

*Group IV.*—144 rats, treated 10 to 14 days with cortisone before exposure to cold and exercise (Table V).

Experiments 10 and 11 were designed to create adrenal suppression in rats preliminary to cold and exercise. This suppression was achieved by administration of cortisone. The dosage for Experiment 10 was 1 mg. of cortisone acetate per rat per day given intramuscularly for fourteen consecutive days. The last cortisone injection was seventy-two hours prior to exposure. The 12 control animals in this experiment received 0.1 ml. of saline solution intramuscularly at the same time as the 12 experimental rats were given cortisone. After 6 hours of exposure to cold and exercise the mortality was 41 per cent; 5 rats died and 7 survived out of a group of 12 rats. Exactly the same results were obtained in the control group.

Experiment 11 followed the same pretreatment schedule as Experiment 10; only the cortisone doage was increased to 2.5 mg. per rat per day. After seven hours of exposure to cold the adrenal-suppressed group of 12 rats had two deaths, or a mortality of 16.7 per cent, as compared to the 12 control animals in which there were 6 deaths or 50 per cent mortality. The difference between these figures was statistically insignificant. The combined values which

TABLE IV

| GROUP | EXPERIMENT NUMBER | AGENT | TREATMENT SCHEDULE | SURVIVED NO. | SURVIVED M. W. GM. | DIED NO. | DIED M. W. GM. | TOTAL NO. | TOTAL M. W. GM. | MORTALITY (PER CENT) | CHI SQ. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| III | 8 | Cortisone | 2.5 mg./r. for 3 days | 21 | 236.19 | 3 | 247.33 | 24 | 237.58 | 12.5 | |
| | | 0.9 per cent NaCl | 0.1 ml./r. for 3 days | 17 | 237.23 | 7 | 235.14 | 24 | 236.62 | 29.2 | 2.02 |
| III | 9 | ACTH | 2 u./r. 2 doses during exposure | 12 | 224.91 | 12 | 209.16 | 24 | 217.04 | 50.0 | |
| | | 0.9 per cent NaCl | 0.1 ml./r. 2 doses during exposure | 13 | 224.53 | 11 | 219.18 | 24 | 222.08 | 45.8 | 0.08 |

TABLE V

| GROUP | EXPERIMENT NUMBER | AGENT | TREATMENT SCHEDULE | SURVIVED NO. | SURVIVED M. W. GM. | DIED NO. | DIED M. W. GM. | TOTAL NO. | TOTAL M. W. GM. | MORTALITY (PER CENT) | CHI SQ. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| IV | 10 | Cortisone | 1 mg./r. 14 days, 3-day pause | 7 | 216.10 | 5 | 210.80 | 12 | 213.90 | 41.0 | |
| | | 0.9 per cent NaCl | 0.1 ml./r. 14 days, 3-day pause | 7 | 219.00 | 5 | 212.00 | 12 | 216.10 | 41.0 | 0.00 |
| IV | 11 | Cortisone | 2.5 mg./r. 14 days, 3-day pause | 10 | 192.50 | 2 | 199.50 | 12 | 193.60 | 16.7 | |
| | | 0.9 per cent NaCl | 0.1 ml./r. 14 days, 3-day pause | 6 | 219.60 | 6 | 221.70 | 12 | 220.70 | 50.0 | 2.66 |
| IV | 10 & 11 | Cortisone | As above | 17 | 202.2 | 7 | 207.0 | 24 | 203.7 | 29.2 | |
| | | 0.9 per cent NaCl | As above | 13 | 219.2 | 11 | 216.4 | 24 | 218.8 | 45.8 | 1.06 |
| IV | 12 | Cortisone | 2.5 mg./r. 2 days, 5-day pause, 3 days | 21 | 211.23 | 3 | 212.00 | 24 | 211.33 | 12.5 | |
| | | 0.9 per cent NaCl | 0.1 ml./r. 2 days, 5-day pause, 3 days | 7 | 221.14 | 17 | 220.88 | 24 | 220.95 | 70.8 | 12.38 |
| IV | 13 | Cortisone | 2.5 mg./r. 10 days, no pause | 21 | 215.66 | 3 | 222.00 | 24 | 216.45 | 12.5 | |
| | | 0.9 per cent NaCl | 0.1 ml./r. 10 days, no pause | 14 | 229.78 | 10 | 232.00 | 24 | 230.70 | 41.7 | 5.17 |

were obtained by pooling Experiments 10 and 11 were even less convincing that adrenal suppression had exerted any influence upon the tolerance to cold during exercise.

In Experiment 12, the pretreatment consisted of intermittent cortisone administration after the design of Experiment 7 (Table III). Since the rats obtained a significant protection to cold resulting from this type of pretreatment in a resting state the same results were to be expected on the exercised animals. The 24 rats of the experimental group were given 2.5 mg. of cortisone acetate intramuscularly to each rat for two days, after which no drug was given for five days. On the eighth day, the cortisone treatment was reinstated and continued for two more days. The animals were then exposed to cold and exercise one hour after the last dose had been given. The 24 control rats received 0.1 ml. of saline solution intramuscularly on the schedule as the experimental group. The exposure time for this experiment was 7 hours, after which time the cortisone-treated group of 24 rats had only 3 deaths or a mortality of 12.5 per cent; whereas the group of twenty-four control rats exhibited 17 deaths or a mortality of 70.8 per cent. Thus, the group prepared by intermittent cortisone administration had a six times smaller mortality than the corresponding control group. To investigate further the role of intermittent cortisone administration, Experiment 13 was carried out. In this experiment the cortisone was administered for ten consecutive days without the five-day pause between two-day priming and the three-day pre-exposure cortisone treatment. Twenty-four experimental rats received 2.5 mg. of cortisone acetate per rat per day given intramuscularly for ten consecutive days. The last dose of cortisone was administered one hour prior to exposure. Again, 0.1 ml. of saline solution per rat per day on the schedule similar to that of the experimental group was the treatment for the 24 control animals. After the exposure to cold and exercise for eight hours the 24 cortisone-treated rats had 3 deaths or a mortality of 12.5 per cent, which equaled the mortality figure in Experiment 12. The control group of 24 rats had 10 deaths with a mortality of 41.7 per cent. This figure is considerably lower than the corresponding figure of 70.8 per cent in Experiment 12. However, the values of 12.5 per cent and 41.7 per cent mortality in two different groups of twenty-four animals are statistically significant and indicate that cortisone administered in the above-mentioned way protected the rats from cold during moderate exercise.

The animals in this investigation were of quite uniform weight. No persistent trend could be detected in the weight between the surviving and the dead rats in either group throughout the experiment. To determine the cause of death during cold exposure the dead animals were autopsied and the lungs were taken for microscopic examination. Macroscopically there were no changes in any one of the intrathoracic or abdominal organs. Microscopic slides of the lungs revealed occasional slight edema and congestion which were interpreted as terminal changes. In no instance was pneumonia encountered.

SUMMARY

The data from the preceding experiments suggest that:

1. The tolerance to cold in rats is significantly greater at rest than during moderate exercise.

2. Short-term cortisone or corticotropin administration prior to and/or during exposure to cold did not appreciably influence tolerance of anesthetized or nonanesthetized rats to cold, neither at rest nor during moderate exercise.

3. Adrenal suppression (medical adrenalectomy) did not significantly alter the tolerance to cold of rats at rest or during moderate exercise.

4. The long-term intermittent cortisone administration prior to exposure to cold definitely increased the tolerance of rats to cold, both at rest and during moderate exercise.

REFERENCES

1. Engel, F. C.: Role of the Adrenal Cortex in Intermediary Metabolism, Am. J. Med. **10:** 556, 1951.
2. Frederickson, D. W., Forsham, P. H., and Thorn, G. W.: The Effect of Massive Cortisone Therapy on Measurements of Thyroid Function, J. Clin. Endocrinol. **12:** 541, 1952.
3. Goldenberg, I. S., Lutwak, L., Rosenbaum, P., and Hayes, M. A.: Thyroid-Adrenocortical Interrelations Following Operation, Surg. Gynec. & Obst. **98:** 513, 1954.
4. Hartman, F. A., Brownell, K. A., and Crosby, A. A.: The Relation of Cortin to the Maintenance of Body Temperature, Am. J. Physiol. **98:** 674, 1931.
5. Hill, S. R., Jr., Reiss, R. S., Forsham, P. H., and Thorn, G. W.: The Effects of Adrenocorticotropin and Cortisone on Thyroid Function; Thyroid-Adrenocortical Interrelationships, J. Clin. Endocrinol. **10:** 1375, 1950.
6. Horwath, S. M.: Response to Cold Following Double Adrenalectomy, Endocrinology **23:** 223, 1938.
7. Horwath, S. M., Hitchcock, F. A., and Hartman, F. A.: Response to Cold After Reduction of Adrenal Tissue, Am. J. Physiol. **121:** 178, 1938.
8. Ingle, D. J., Nezamis, J. E., and Morley, E. H.: Effect of Cortisone Upon the Work Output of Adrenal Ectomized Rat, Am. J. Physiol. **166:** 504, 1951.
9. Leblond, C. P., and Gross, J.: Effect of Thyroidectomy on Resistance to Low Environmental Temperatures, Endocrinology. **33:** 155, 1943.
10. Marine, D., and Baumann, E. J.: Effect of Suprarenal Insufficiency on Rabbits, Am. J. Physiol. **57:** 135, 1921.
11. Pashkis, K. E., Epstein, D., Cantarow, A., and Friedler, G.: Influence of Adrenal Hormones on Thyroid Function in the Hypophysectomized Rat (abstracts), J. Clin. Endocrinol. **12:** 939, 1952.
12. Selye, H., and Dosne, C.: Physiological Significance of Compensatory Adrenal Atrophy, Endocrinology **30:** 581, 1942.
13. Stevens, C. E., D'Angelo, S. A., Pashkis, K. E., Cantarow, A., and Sunderman, F. W.: Effect of Cold on Pituitary-Thyroid-Adrenal Relationship in the Guinea Pig, J. Clin. Endocrinol. **13:** 872, 1953.
14. Szilagyi, D. E., McGraw, A. B., and Smyth, N. P. D.: The Effect of Adrenal Cortical Stimulation on Thyroid Function, Ann. Surg. **136:** 555, 1952.
15. Tyslowitz, R., and Astwood, E. B.: The Influence of the Pituitary and Adrenal Cortex on Resistance to Low Environmental Temperatures, Am. J. Physiol. **136:** 22, 1942.
16. Woodbury, D. M., Ghosh, B. N., and Sayers, G.: Modification of TSH Action by ACTH and Cortisone in Hypophysectomized Rats (abstracts), J. Clin. Endocrinol. **11:** 761, 1951.

# GRACILIS MUSCLE TRANSPLANT FOR RECTAL INCONTINENCE

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IN INFANCY, before the development of cortical centers, and completion of the connecting pathways, voluntary or cerebral control over both micturition and defecation is absent. As a result, the bladder and rectum are emptied at irregular intervals. With the development and completion of the pathways and higher centers, a cerebral or suprasegmental control over the spinal cord reflex is developed so that in the adult, under normal conditions, this reflex activity is in complete abeyance to this supranuclear control and remains so until it is convenient to evacuate the rectum or bladder voluntarily. Clinical studies[11] and animal experiments[1, 5] have localized the reflex activity of both defecation and micturition to the second, third, and fourth sacral segments. Destruction of these sacral segments or cauda equina results in loss of sensation of both the bladder and the rectum and, as a result, reflex evacuation occurs. Since the bladder and the lower rectum have the same nerve supply, neurogenic incontinence of both urine and feces is the rule. Bladder incontinence is always accompanied by rectal incontinence in neurogenic abnormalities, unless the patient, child or adult, is taught to evacuate the bladder every two hours, or less, by straining and manual pressure so that the bladder is emptied to a sufficient degree so that actually there is no incontinence of urine. However, there is no satisfactory comparable training program or mechanism for the rectum.

*Incontinence in Children,* exclusive of traumatic lesions, is most frequently due to spina bifida, meningocele, or to some congenital malformation involving the second, third, and fourth sacral segments which supply and control the rectum and anus. Hence, with the absence of sensation, they are not conscious of the passage of feces. However, when the rectum is plugged for 24 to 48 hours, a definite sensation of abdominal fullness and distention is felt.

When the nerve supply to the perineum is absent (neurogenic incontinence) it is upon the perception and recognition of these sensations of fullness and distention of the sigmoid and colon that the success of this operation and the maintenance of rectal continence depend, whether in child or adult.

Distention stimuli of the colon are thought to travel in segmental nerves in the peritoneum, and by afferent fibers through the mesentery from the

Received for publication Sept. 12, 1955.

lower thoracic and upper lumbar nerves, without involvement of sympathetic or parasympathetic pathways. While the mode of transmission of these stimuli is of physiologic and academic importance, that they occur and are present is of extreme importance in the present consideration. Both children and adults with perineal anesthesia can readily feel and tell when the sigmoid is distended. The pain of spasm also occurs and is readily recognizable. It is upon the perception and recognition of these sensations that the success of the gracilis transplant operation depends, when the nerve supply is absent and the perineum is anesthetic.

*Incontinence in Adults,* excluding those patients with congenital or traumatic abnormalities of the spinal column and cord, is due, in most instances, to trauma resulting from childbirth, operations, or injuries; or is the result of radiation or the injection of sclerosing solutions. There are many factors and causes which may be responsible for impaired rectal sphincter action and partial or total incontinence. It is not our intent to discuss the causes of incontinence, but rather to present an operation to correct it. This procedure is applicable to many types of total incontinence, both in children and in adults, and it is not dependent upon the continuity or integrity of the nerve supply or the musculature of the perineum.

## ANATOMIC AND PHYSIOLOGIC CONSIDERATIONS

*The external anal sphincter* is subcutaneous and is attached anteriorly to the perineal muscles and posteriorly to the coccyx; it is divided into a superficial and deep lamina. The muscle fibers may extend anteriorly and posteriorly on each side of the anus to insert into the perineal body; or, they may encircle the anal orifice either anteriorly or posteriorly or both, and function from a relatively fixed point, such as the coccyx or central tendon of the perineum, depending upon the completeness of the anal circumference which they encompass. It is seen, then, that the external sphincter does not possess a fixed anatomic pattern, but the small bundles of muscle fibers find their way by diverse routes to variable fixed points in the perineum to exert their action.

*The motor nerves* to all the superficial perineal muscles, to the levator ani, and to the external sphincter of the bladder are innervated by the internal pudendal nerves. These are bilateral somatic fibers which take origin from the anterior primary divisions of the third and fourth sacral nerves. They leave the pelvis through the lesser sciatic notch and run forward in Alcock's canal to supply the perineum. Integrity of the internal pudendal nerves may be determined on the motor side by the voluntary activity of the external sphincter and the bulbocavernosus muscle. The inferior hemorrhoidal branches follow a pattern similar to that of the vascular arbor and provide innervation through each of four sectors to include the entire circumference of the anus.

*Sensory nerve* continuity is determined by the sensation in the saddle area of the perineum. Since the innervation is essentially the same, the activity of the external sphincter of the rectum and anus parallels that of the external sphincter of the bladder.

The pelvic *parasympathetic nerves* have their origin in the second, third, and fourth sacral segments, and pass by way of the cauda equina through the primary divisions of the corresponding sacral nerves, which join the hypogastric plexus before being distributed to the bladder and rectum. The most consistent branches arise from the third and fourth sacral nerves. These fibers are made up of preganglionic efferent and afferent fibers from the parasympathetic division of the autonomic nervous system.

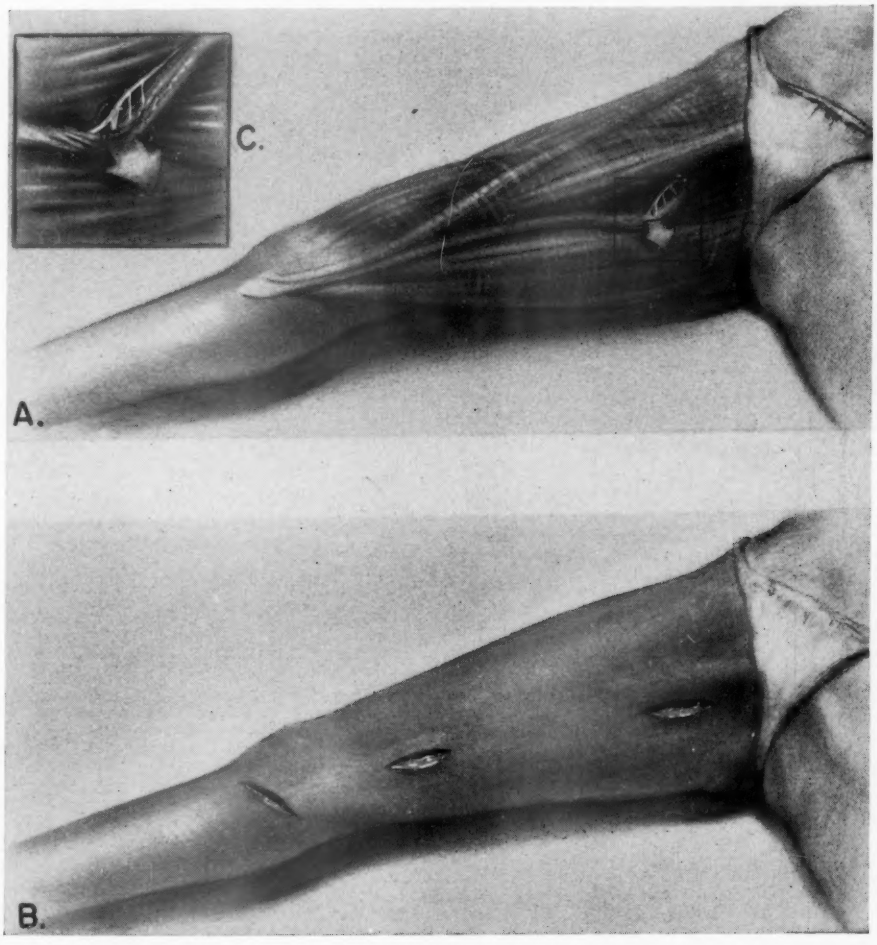


Fig. 1.—*A*, The gracilis is the most superficial muscle along the inner aspect of the thigh, being located at its origin just medial to the tendon of the adductor longus. It arises from the lower half of the symphysis and pubic arch and extends below the knee to insert into the tibia in dovetail fashion. *B*, The highest incision in the thigh is made just medial to the tendon of the adductor longus in the adductor-gracilis groove or trough. The proximal part of the tendon is mobilized with finger dissection to avoid injury to the neurovascular bundle which enters from the lateral side (Fig. 1, *C*). A second incision is made parallel to the muscle over its lower third. Traction placed on the muscle through the highest incision will disclose the path of the muscle. A third incision is made in an oblique direction along the upper and medial aspect of the tibia to preserve the dovetail insertion of the gracilis into the periosteum of the tibia. All incisions are connected by subcutaneous tunnels through which the muscle is mobilized. *C*, The innervation ($L_{2,3,4}$) and blood supply (*profunda femoris*) enter the gracilis high on its lateral side as a neurovascular bundle. Care should be exercised to avoid injury to it.

*The innervation of the colon* is not understood clearly. However, it is thought that distention stimuli travel in segmental nerves in the peritoneum,

and by afferent fibers through the mesentery from the lower thoracic and upper lumbar nerves without involvement of sympathetic or parasympathetic pathways.[18, 19]

*The blood supply* to the anal orifice and the anterior two-thirds of the sphincter is derived from the perineal artery, a branch of the internal pudendal which anastomoses above with the middle hemorrhoidal artery. The posterior one-third receives its blood supply from the inferior hemorrhoidal artery.

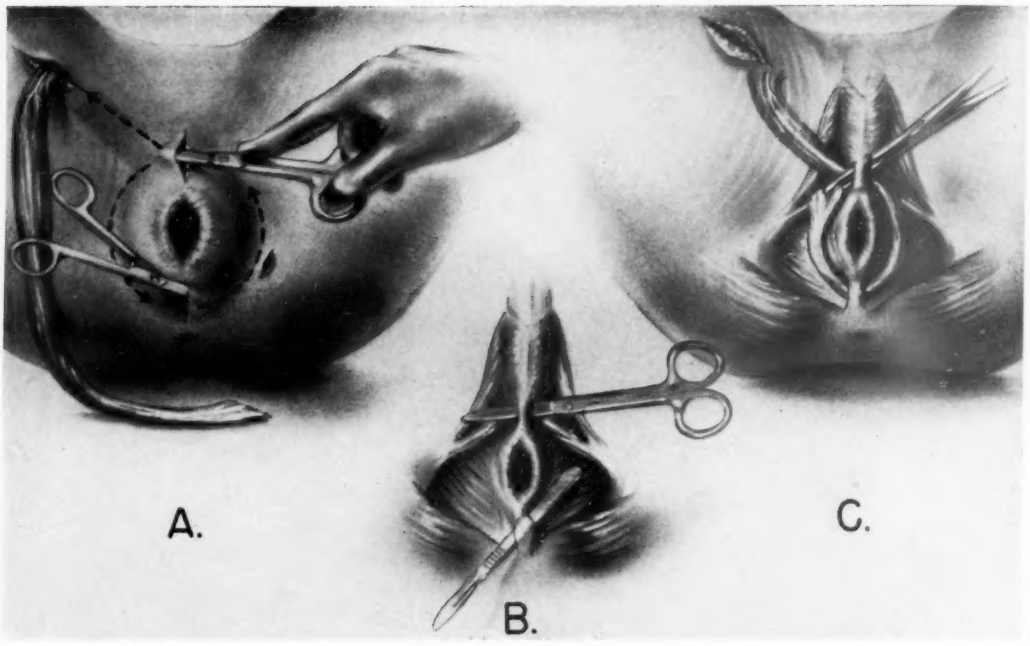


Fig. 2.—*A*, With absence of muscle tone and structural support, the perineal floor will bulge when the patient is placed in exaggerated lithotomy position. Incisions are made in the anterior (12 o'clock) and posterior (6 o'clock) commissures, being careful to avoid injury to the raphae. A subcutaneous tunnel is made around the anus. A tunnel is also made to connect the highest incision in the thigh with the incision at 12 o'clock. *B*, When possible, pulleys are constructed from the anterior and posterior raphae. They are not essential, however. *C*, The gracilis tendon and muscle are threaded through the tunnels and beneath the pulleys, if they have been constructed.

*The gracilis muscle* is ideally suited and readily adaptable for transplantation: it is the most superficial muscle on the medial or inner aspect of the thigh. It arises from the margins of the lower half of the pubic symphysis and the upper half of the pubic arch (Fig. 1, *A*). The origin of the muscle per se cannot be palpated distinctly. However, when the thigh is abducted and the lower leg is flexed to 90 degrees at the knee, the tendon of the adductor longus muscle stands out prominently and can be felt as a dense, cordlike structure two or three fingerbreadths medial to the fossa ovalis (Fig. 1, *A*). With the extremity in this position, (thigh abducted and lower leg flexed) a groove or hollow can be felt just medial to the adductor tendon. The uppermost portion of the gracilis muscle is located in this depressed area or trough. Now, with the examining fingers arranged vertically in this anatomical gutter, as an

assistant extends the lower leg, the fingers will be ejected from this gutter as the tendon of the gracilis muscle tightens and obliterates the space between it and the adductor muscle. This space is of considerable importance since the neurovascular bundle enters the gracilis muscle here; also, an operative incision (Fig. 2, *A*) will be placed just medial to it to expose the proximal end of the gracilis with its entering nerves and blood vessels (Fig. 1, *B* and *C*).

The fibers of the gracilis run downward vertically, being quite broad above, and narrow and tapering below (Fig. 1, *A*). The muscle is surprisingly long, measuring 16 inches or more in length in an adult. The muscle fibers converge above the level of the knee, at approximately the lower third of the thigh, to end in a rounded tendon which passes behind the medial condyle of the femur, then it curves around the medial condyle of the tibia, where it becomes flattened and inserts in dove- or fishtail fashion into the tuberosity and medial surface of the body of the tibia, just behind the tendon of the sartorius. Both the type and the location of the insertion of the gracilis are of importance (Figs. 1, *A*, and 2), because this tendon terminal will be anchored to a fixed point when the new sphincter is constructed.

*The nerve supply* of the gracilis is derived from the obturator ($L_2$, $L_3$, $L_4$) which enters the upper fourth of the muscle as a main trunk and three branches.[9] Several accessory branches may enter at lower levels. The *blood vessels* from the *profunda femoris* enter the muscle with the main nerve trunk, from the lateral side, as a neurovascular bundle (Fig. 1, *A*). Care should be exercised to avoid injury to the bundle when the muscle is mobilized. The neurovascular trunk is seen laterally when the upper fourth of the gracilis is retracted medially (Fig. 1, *C*). Since the nerve and blood supply enter the muscle at a high level, transplantation is thereby facilitated, and without endangering its function or vitality. The gracilis adducts and flexes the thigh as it is rotated inward.

## GRACILIS MUSCLE TRANSPLANT

*Preparation and Preoperative Studies.*—Preparation begins about three days prior to operation with a high colonic flushing. Roentgenograms of the chest, abdomen, lumbar vertebrae, sacrum, and pelvis are obtained to confirm or rule out structural abnormalities. A barium enema is obtained, and this is followed by a repeat flushing to empty the colon. The patient is placed on a low-residue diet. The preoperative use of antibiotic agents, intestinal and urinary tract antiseptics is empirical and must be individualized. Neomycin is a quick-acting intestinal antiseptic, but it may cause diarrhea. Terramycin works somewhat more slowly, requiring about three days for effective "sterilization" of the intestinal tract.

Expert urologic consultation and studies are most important. It is almost axiomatic that if an incontinent or toneless bladder is catheterized, the urinary tract will become infected. Therefore, the urologist should perform the catheterization, if indicated, because of the danger of introducing infection. The consultant will obtain pyelograms and will determine the status

of the genitourinary system. It should be emphasized that in neurogenic incontinence, the rectum and bladder are affected together and, since they have the same nerve supply, incontinence of one does not occur without the other.

The neurologist or neurosurgeon will advise regarding motor and sensory innervation, loss, and levels, while the orthopedist or physical therapist will perform muscle evaluation studies. If one extremity or gracilis is stronger than the other, the stronger muscle should be selected for transplant.

*Operation.*—Beginning above the ankles, both legs and thighs, the perineum, the inferior and lateral aspects of the buttocks, and the abdomen to the umbilicus are prepared as a sterile field. The urologic consultant will have advised the type of catheter, if any, to be inserted into the bladder.

If the right gracilis muscle is to be transplanted, the right thigh is abducted while the lower leg is flexed to 90 degrees at the knee. The gutter between the tendons of the adductor longus and gracilis muscles is palpated. With the thigh abducted and the lower leg alternately flexed and extended, the adductor-gracilis gutter appears and disappears as the gracilis is tightened and relaxed.

*Thigh incisions.*—With the fingers of the left hand placed medial to the adductor tendon and in the groove between it and the gracilis muscle, a vertical incision approximately two inches in length is made directly over the upper fourth of the gracilis muscle (Fig. 1, *B*). The incision is deepened through the subcutaneous fat to expose the fascia, which is incised. The muscle is then freed inferiorly in its canal by blunt finger dissection. With the index finger hooked around the muscle belly, tension is exerted upon the muscle and, while doing so, the path of the gracilis along the inner aspect of the thigh is disclosed.

*A second incision,* approximately two inches in length, is made parallel with the long axis of the muscle over its lower third and just above the knee (Fig. 1, *B*). At this point, the gracilis is situated just posterior to the sartorius muscle. Here also the gracilis becomes tendinous. After identifying the oval tendon of the gracilis, the muscular portion is freed superiorly by blunt finger dissection. It may be necessary to incise the fascia along the muscle to free it completely. The lower leg is then flexed to 90 degrees at the knee. This relaxes the gracilis tendon, which is then freed by blunt finger dissection inferiorly as it passes behind the medial condyle of the femur, the knee joint, and curves around the medial condyle of the tibia. This part of the dissection is "blind"; however, atraumatic freeing of the tendon is facilitated by adducting the thigh and flexing the lower leg.

*A third incision* (Fig. 1, *B*) approximately two inches in length is made in an oblique direction along the upper and medial aspect of the tibia, where the tendon of the gracilis becomes flattened and inserts into the body of the tibia in dovetail fashion below the condyle and tuberosity of the tibia. Traction on the muscle through the incision in the lower thigh will identify the termination of the gracilis, so that the entire fishtail insertion can be preserved with its the semimembranosus, and in front of the semitendinosus tendons. This incision should be adequate, and enlarged if necessary, to expose the termination

of the gracilis, so that the entire fish-tail insertion can be preserved with its periosteal attachment to the tibia. Care and attention to this detail will facilitate anchoring of this tendinoperiosteal end of the gracilis to the periosteum overlying the tuberosity of the ischium or the inguinal ligament of the opposite side. If necessary, this incision may be extended in hockey stick fashion.

The freed insertion of the gracilis is then made to present through the incision along the lower third of the thigh. The tendon is handled with meticulous care, and is kept warm and moist with saline sponges. With a finger hooked around the origin of the muscle, through the highest incision in the thigh, the entire muscle is drawn through the subcutaneous tunnel and is made to present through the highest incision in the thigh. Finger or blunt scissors dissection will suffice to sever any fascial bands which adhere to the muscle. The lower incisions are closed in layers using interrupted sutures of silk, after perfect hemostasis has been obtained.

Extreme care is exercised to avoid injury to the obturator nerve ($L_2$, $L_3$, $L_4$) and the vessels from the *profunda femoris* which enter the highest part of the muscle as a neurovascular bundle from the lateral aspect (Fig. 1, *A* and *C*). The obturator nerve enters as a main trunk and three or four branches. The use of a nerve stimulator may be advantageous to identify the nerve.

*Perioneal Incisions.*—The foot end of the operating table is lowered, the legs and thighs are flexed and placed in an exaggerated lithotomy position to expose the entire perineum. Small superficial incisions are then made in the anterior and posterior commissures at 12:00 and 6:00 o'clock, beginning about one inch from the mucocutaneous junction (Fig. 2, *A*). The incisions are deepened on each side of the raphae, care being exercised to avoid injury to the raphae, for they will be used subsequently as pulleys (Fig. 2, *B*). In some instances, the raphae are poorly developed, and pulleys cannot be made.

A subcutaneous tunnel is made around the anus in the adipose layer, using a blunt scissors (Fig. 2, *A*). The tunnel should be of sufficient size to admit the index finger with ease. The undermining should extend almost to the mucocutaneous junction. When the perineum lacks innervation or muscular support, the entire floor may bulge quite markedly; the anus may be patulous and the rectal mucosa may prolapse to a degree sufficient to require the insertion of a small rectal plug.

A subcutaneous tunnel is now made to connect the incision at 12:00 o'clock with the highest incision in the thigh (Fig. 2, *A*). This tunnel should be of sufficient size to admit two fingers freely, to allow the muscle to move and glide freely, and without fear of strangulation.

The gracilis muscle is then threaded through the thigh to perineum tunnel. As the muscle is placed under tension, the neurovascular bundle will be seen to enter from the deep lateral aspect near the origin of the gracilis (Fig. 1, *A* and *C*). If it is not seen, then the muscle has not been mobilized high enough. If it has been possible to form a pulley at 12:00 o'clock, the tendon and muscle are then threaded beneath it. The use of pulleys at 12:00 and 6:00 o'clock may

give additional support to the perineal floor in cases of neurogenic incontinence where the nerve supply to the perineum is absent. However, when pulleys are used, it is of importance that the space beneath them be adequate and of sufficient size to allow the muscle to glide freely and without fear of strangulation. The use of pulleys in post-traumatic or postoperative incontinence (childbirth injuries, following operations for hemorrhoids or fistulas, and so forth, when there is otherwise good perineal support, the formation and use of pulleys is empirical and must be individualized. If good pulleys can be made, then use them. Otherwise abandon the idea, for they are not absolutely necessary.

The tendon and muscle are now threaded around the anus to make a complete circle: in a clockwise direction if the right gracilis is being transplanted, and in a counterclockwise direction if the left gracilis is used. The muscle and tendon are brought through the incision at 6:00 o'clock (and beneath the posterior pulley if one has been made) by inserting a Kelley clamp from one incision to the other, and grasping either the periosteal insertion of the tendon itself or a suture which has been inserted into it. The tendon and muscle are now drawn taut to take up the slack. With an assistant holding the tightened muscle with a sponge moistened with warm saline, the tendon is threaded through the subcutaneous tunnel from 6:00 to 12:00 o'clock. The distal tendon is now passed posterior and beneath the body of the muscle at 12:00 o'clock, regardless of whether or not an anterior pulley has been used (Fig. 2, *C*).

The highest incision of the thigh, as well as those at 12:00 and 6:00 o'clock in the raphae, are now closed in layers using interrupted sutures of 4-0 silk. Some observers have expressed both concern and surprise that silk would be buried subcutaneously in the perineum. However, the perineum, like the face and oral cavity, possesses marked local immunity and resistance, and no untoward effect has been noticed following the subcutaneous implantation of silk. However, meticulous care should be exercised in the closure of the subcutaneous tissues and skin, regardless of the composition of the sutures which are used.

*Anchoring the Gracilis Tendon.*—The tendinoperiosteal end of the gracilis may be anchored either to the periosteum of the ischium and levator ani muscle, or it may be anchored more easily to the medial end of the inguinal ligament (Poupart), the lacunar ligament (Gimbernat), or to the fixed tendinous origin of the adductor longus. It is of importance to remember that the tendon end is always anchored on the opposite side to maintain the central position of the anal orifice and to prevent it from being pulled off sides. If the patient is slender, anchorage of the tendon to the levator ani and periosteum of the tuberosity of the ischium is quite easy and is performed in the following manner.

A transverse incision, approximately two inches in length, is made directly over the tuberosity of the ischium on the side opposite the muscle transplant. This incision will be located at approximately 4:00 o'clock with the thighs flexed in exaggerated lithotomy position. The incision is deepened to expose the tuberosity of the ischium as well as the lateral aspect of the

levator ani muscle (Fig. 3, *A*). A periosteal flap or pulley is elevated from the tuberosity of the ischium. A pulley is also made from a heavy bundle of the levator ani. The dovetail tendinoperiosteal insertion of the gracilis is then split for a centimeter or more. One half of the dovetail is then anchored with sutures of silk either around the periosteal pulley or directly into a periosteal flap over the prominence of the ischium. The remaining half of the dovetail is anchored beneath and around a pulley of levator ani (Fig. 3, *B*), using sutures of silk.

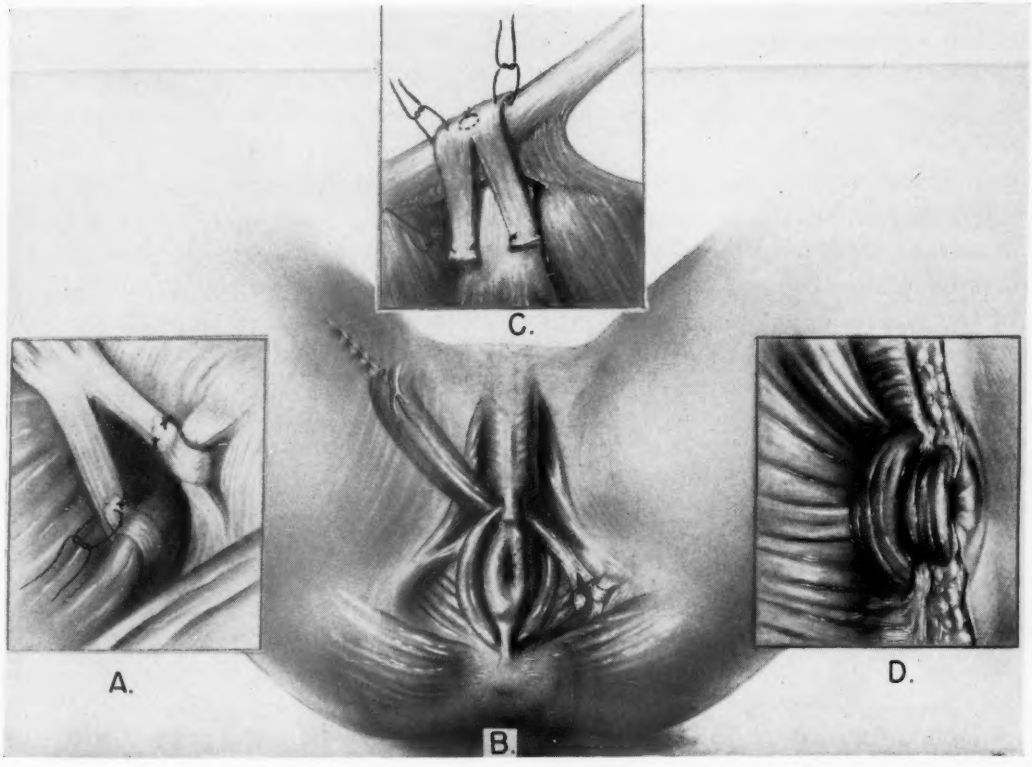


Fig. 3.—*A* and *B*, The dovetail tendinoperiosteal insertion of the gracilis is split to form a Y. If the gracilis is to be anchored into the tuberosity of the ischium on the opposite side, an incision is made directly over the tuberosity at approximately 3 to 4 o'clock (Fig. 4, *B*). One end is anchored around a pulley or a periosteal flap elevated from the tuberosity of the ischium. The remaining limb of the dovetail is anchored around a pulley or bundle of levator ani muscle, using sutures of silk. *C*, In heavy or obese patients, it is easier and better to anchor the gracilis to the adductor tendon or to the lacunar ligament. An incision is made in the groin on the side opposite the transplant. A subcutaneous tunnel is formed to connect it with the incision at 12 o'clock. The tendon is threaded through the tunnel, and beneath the lacunar ligament or tendon of the adductor on the opposite side. The gracilis tendon is then anchored to itself and to the ligament on each side, using sutures of silk. *D*, The anal orifice is constricted and closed by a collar of contractile muscle. Sufficient tension should be placed on the gracilis to insure that the orifice is very tight—like a cervix. Remember that the orifice must be air- and watertight and must be able to withstand considerable pressure upon it.

In patients who are heavy or obese, it is somewhat easier to anchor the tendon end to the medial end of the inguinal ligament, the lacunar ligament or the fixed heavy portion of the adductor longus tendon of origin, on the side opposite the muscle transplant (Fig. 3, *C*). The tendon is anchored in the following manner. An incision, approximately two inches in length, is made

just below the fold of the groin, over the medial end of the inguinal (Poupart) or lacunar (Gimbernat) ligament. The incision is deepened to expose the ligament just lateral to the pubic tubercle, as the spermatic cord in the male is retracted superiorly. By retracting the inferior skin edge downward, the adductor longus tendon is exposed. A subcutaneous tunnel is then formed by finger or blunt scissors or clamp dissection to connect this incision in the groin with the incision at 12:00 o'clock in the perineum. A pulley or tunnel is made beneath the lacunar ligament or the adductor tendon. The tendon end of the gracilis is then pulled through the subcutaneous tunnel into the groin; then beneath and over the pulley of the lacunar ligament or the tendon of the adductor longus. The tendon end of the gracilis is anchored securely both to itself and to the lacunar ligament on each side (Fig. 3, *C*), using sutures of silk. The incision in the groin is then closed in layers using interrupted sutures of silk.

Regardless of whether the tendinous end of the gracilis is anchored over the tuberosity of the ischium, to the adductor tendon, or to the ligament in the groin, the final fixation of the tendon is not decided upon nor fixed until the legs have been brought down into line with the body, and then the tendon end of the muscle is drawn taut to make absolutely sure that the anus is not only snug but very tight. Do not fail to remove the rectal plug, if one has been inserted, before testing for tightness. Since the anal orifice must be both air- and watertight, it is almost impossible to make it too tight. When attempting to insert the index finger, a cervixlike barrier should be encountered. If it is possible to insert the finger, the muscle has not been tightened sufficiently. The patulous anus and the relaxed perineum are now tight and drawn inward between the buttocks, and the central position of the anus is maintained.

All operative incisions are closed in layers with sutures of silk. The perineal incisions are sealed with collodion; no perineal dressing is applied. A snug compression dressing is applied to the thigh to prevent hematoma formation. The urologic consultant will advise regarding the insertion or removal of a catheter.

*Postoperative Care and Training.*—Postoperative pain is not profound and only moderate sedation is necessary. The patient is placed on a liquid diet for the first several days, and then a low-residue diet for a period of five to seven days. At this time, well-balanced meals are begun, supplemented with mineral oil at bedtime.

The incisions will have healed so that the sutures may be removed at the end of one week.

Patients with neurogenic incontinence will become conscious of a feeling of abdominal fullness, usually after five to seven days. It is of interest to note that in children with incontinence due to spina bifida or meningocele, this is the first time that they have ever experienced the sensation of distention. When it occurs, the patient is placed upon a commode or training seat, and with the thighs adducted and the trunk flexed, he is taught to relax the perineum and apply kneading, manual pressure to the lower abdomen. If

cramps are felt, it is possible that the gracilis cuff (Fig. 3, *D*) is too tight. Gentle finger massage and dilatation will cause it to relax. This initial training period, and others to follow each morning, either before or after breakfast, must not be hurried. From the psychologic standpoint, it is of extreme importance, and especially so in children, that this first postoperative bowel movement occurs while sitting at stool, rather than as a mass evacuation in bed. Subsequent daily training periods should be scheduled at 8:30 or 9:00 o'clock each morning. Upon awakening, a child is given one-half glass of warm water to which has been added one-half teaspoon of table salt. Adults receive a full glass of warm water to which has been added a full teaspoon of salt. We have found that this will produce the desired cathartic effect within about an hour. If an impaction should occur, an oil retention enema may be necessary. This is preferable to attempting to remove it manually, which might cause separation of the perineal incisions. The patient, child or adult, is usually quite well trained and ready for discharge in approximately two weeks. Studies indicate that flexion and extension of the thigh do not affect the tonicity of the reconstructed orifice. Abduction of the thigh, however, tightens the opening, while adduction of the thigh and flexion of the trunk, as at stool, relax the entire perineal floor and anal orifice.

## DISCUSSION

In patients with neurogenic incontinence and anesthesia of the perineum, due to interruption of the nerve supply to the perineum, rectum, and bladder—the result of spina bifida, meningocele or paraplegia—the gracilis sling or transplant operation will restore voluntary, controlled continence. However, it is not automatic and subconscious as in the normal sphincter mechanism. This reconstructed sphincter is always tight, except when it is relaxed purposefully. However, in patients with rectal incontinence due to absence or division of the sphincter mechanism, but who have good perineal sensation, the gracilis sling transplant will restore essentially normal, voluntary, and automatic control.

Thirty-four patients have been operated upon with gratifying results. In each instance, the patient has developed continence of both feces and gas. Eighteen patients were children who ranged in age from 3 to 14 years. Fourteen were operated upon to correct neurogenic incontinence; two for imperforate anus, and one, a child of 3 years, for traumatic avulsion of the perineum when the child was attacked by a sow when he ventured too near her litter. Of the 16 adult patients, ranging from 20 to 72 years, 3 were paraplegics, 2 had perineal colostomies, and the remaining 11 patients had developed incontinence following operations upon the rectum and anus. One woman, a 63-year-old diabetic with massive prolapse and incontinence, was operated upon a second time. There have been no purulent or gross infections, and no complications except for occasional slight separation of the skin edges of the incisions at 6:00 and 12:00 o'clock in the perineum, which may be anticipated in those patients who have had many previous operations in and around the anal orifice, and in whom extensive scarring is present.

Our patients, both children and adults, were essentially social outcasts except within their immediate families. Possibly resulting from this social ostracism, they were extremely anxious to learn to use the new sphincter mechanism, and continence developed in each instance. Several patients have been followed for more than seven years.

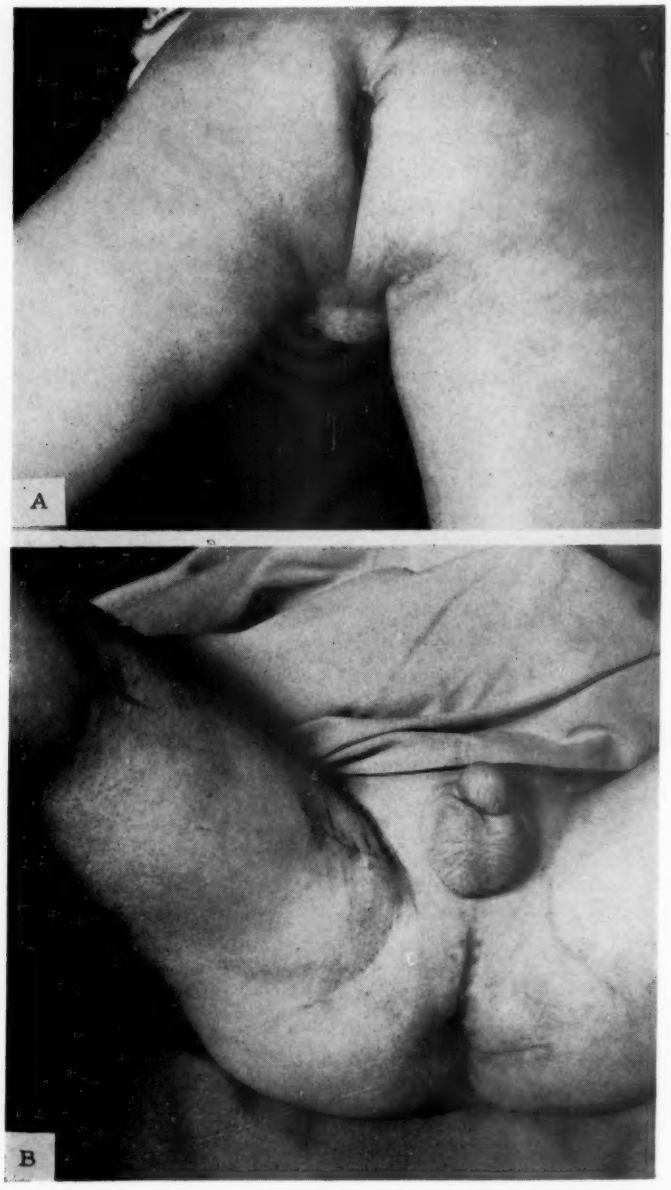


Fig. 4.—*A*, A 4-year-old boy with rectal incontinence and prolapse due to spina bifida. The perineal floor bulged due to lack of innervation and muscular support. Prolapse occurred because the orifice was patulous. *B*, Rectal continence was restored by transplanting the right gracilis muscle which was anchored to the tuberosity of the ischium on the left side. Postoperative photograph was taken one year following operation.

In children with incontinence due to neurogenic abnormalities (spina bifida, meningocele), or those with structural abnormalities of the perineum

(imperforate anus), we believe that the optimum age for the gracilis transplant operation is between four and five years. This will spare the child psychologic insults, abuse, and ostracism at kindergarten or school.

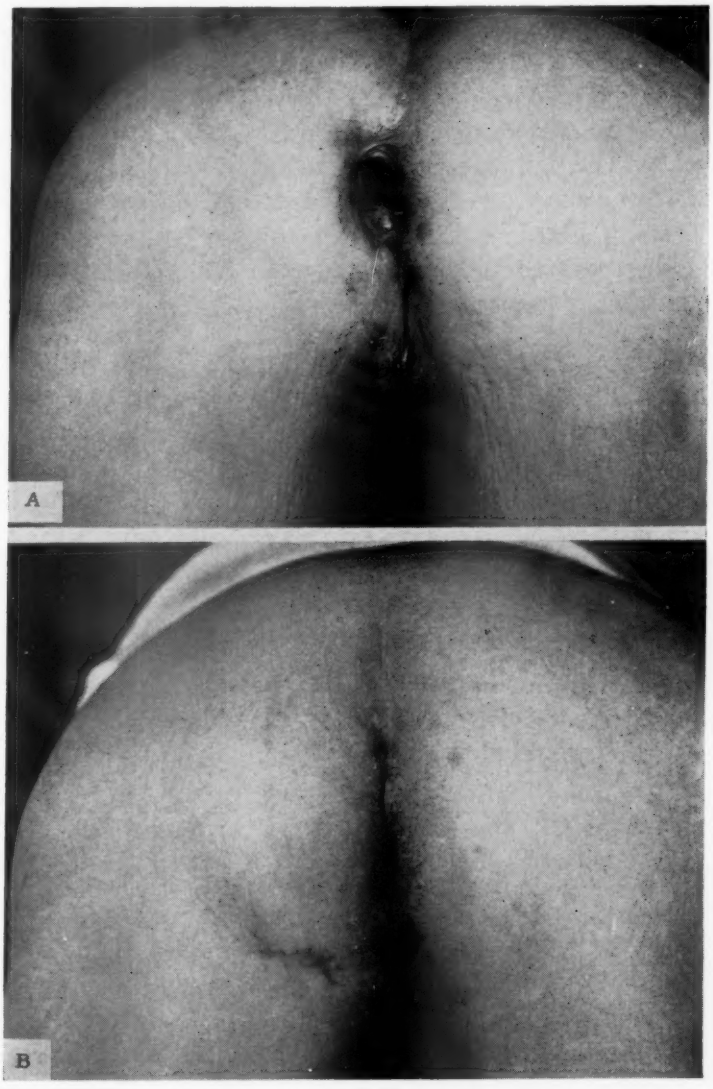


Fig. 5.—*A*, A 55-year-old woman with rectal incontinence resulting from many operations on the orifice and canal. The rectum prolapsed when standing erect. *B*, Rectal continence was restored by transplanting the gracilis muscle. Postoperative photograph was taken three years following the gracilis sling operation.

*Other Operations for Incontinence.*—In 1932, Dr. Harvey Stone[15, 16] introduced his fascia loop operation: 2 loops of preserved fascia encircle the anus from opposite directions. The free or open ends are anchored into the gluteus maximus of the opposite side. The anal orifice is thus enclosed in a double ring of fascia. In appraising the operation, Stone and McLanahan[17] stress that before this operation can have any chance of success, the gluteal muscles must be properly innervated and able to contract voluntarily, the individual

must possess the intelligence to use the muscles to contract the anal canal, and the patience to practice this contraction frequently. Chittenden[4] used bilateral muscle flaps from the glutei which were sutured anterior to the rectum. Bistrom[2] used bilateral flaps from the glutei which were long enough to overlap the anal orifice; a hole was made in the distal end of each flap, through which the anus was drawn. Operations designed for repair of the divided muscle have been introduced by Gobells,[6] Izquierdo,[10] Sistrunk,[13] Steindl,[14] Hirschmann,[8] and others. These operators had as their aim the approximation by suture of the severed muscle ends, which had been divided by injury or operation. In instances of recent injury this can be accomplished, but the majority of cases are seen late, and in the meantime, the muscle has retracted, atrophied, and degenerated into fibrous tissue. As a result, these operations have not been uniformly successful.

## CONCLUSIONS

The gracilis transplant operation has been performed on 34 patients; 18 patients children and 16 adults. Except in one instance, the children had been incontinent since birth because of imperforate anus, spina bifida, meningocele, or some neurogenic malformation involving the rectum and perineum. The 16 adult patients ranged from 20 to 72 years; 3 were paraplegics, 2 had perineal colostomies, and the remaining 11 patients, were incontinent following operations upon the anus or rectum. Rectal continence was restored in all patients.

The technique of the gracilis sling or transplant operation is described. While the tendinoperiosteal insertion of the gracilis may be anchored to either the tuberosity of the ischium, the adductor tendon, or the inguinal ligament on the opposite side, the anchorage point of choice in heavy individuals is in the groin.

A gracilis transplant operation has been devised to correct urinary incontinence. Three patients have been operated upon and urinary continence has been restored. We hope to be able to report on this operation in the very near future.

## REFERENCES

1. Barrington, F. J.: The Physiology of Micturition, Quart. J. Exper. Physiol. **8**: 33, 1914.
2. Bistrom, O.: Plasticher Ersatz des M. Sphincter Ani, Acta chir. scandinav. **90**: 431, 1944.
3. Capmal, André: Tentatives de Rétablissement de la Continence de l'Anus Périnéal Aprés Amputation du Rectum. Avignon, 1953, Maison Aubanel Père.
4. Chittenden, A. S.: Sphincter Muscle Reconstruction, Ann. Surg. **92**: 152, 1930.
5. Elliott, T. R.: The Innervation of the Bladder and Urethra, J. Physiol. **35**: 367, 1907.
6. Gobells, R.: Method of Forming New Anal Sphincter, Arch. klin. chir. (Kongressbericht) **148**: 612, 1927.
7. Gonzalez, Miguel F.: Incontinencia del Anal Operacion de Pickrell, Arch. Soc. cirujanos de Chiles **5**: 757, 1953.
8. Hirschmann, L. J.: Establishment of Continent Anal Sphincter by Pediculated Innervated Myoplasty, Tr. Am. Proct. Soc. **36**: 178, 1935.
9. Hollinshead, W. H., and Markee, J. E.: The Multiple Innervation of Limb Muscles in Man, J. Bone & Joint Surg. **28**: 721, 1946.
10. Izquierdo, J.: Artificial Anal Sphincter, Deutsche. Med. Wchnschr. **52**: 795, 1926.
11. McLellan, F. C.: The Neurogenic Bladder. Springfield, Ill., 1939. Charles C Thomas, Publisher.

12. Pickrell, K., Masters, F., Georgiade, N., and Horton, C.: Rectal Sphincter Reconstruction Using Gracilis Muscle Transplant, Plast. & Reconstr. Surg. **13**: 46, 1954.
13. Sistrunk, W.: Plastic Surgery Operation for Extensive Laceration of Anal Sphincter, Ann. Surg. **85**: 185, 1927.
14. Steindl, H.: Surgery—In Relation to Continence, Wien. med. Wchnschr. **79**: 1516, 1538, 1929.
15. Stone, H. B.: Plastic Operation for Anal Incontinence, Arch. Surg. **18**: 845, 1929.
16. Stone, H. B.: Plastic Operation for Anal Incontinence, Arch. Surg. **24**: 120, 1932.
17. Stone, H. B., and McLanahan, S.: Results With Fascia Plastic Operation for Anal Incontinence, Ann. Surg. **114**: 73, 1941.
18. White, J. C.: Sensory Innervation of the Viscera, Proc. A. Research Nerv. & Ment. Dis. **23**: 373, 1943.
19. Wolf, H. G., and Wolf, S.: A Monograph of American Lectures in Physiology. Springfield, Ill., 1948, Charles C Thomas, Publisher.

# TOTAL CARDIAC BY-PASS IN HUMANS UTILIZING A PUMP AND HETEROLOGOUS LUNG OXYGENATOR (DOG LUNGS)

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MAINTENANCE of respiratory function with isolated mammalian lungs has been reported from experimental laboratories since the nineteenth century. Recently[1-3] several investigators successfully employed homologous lungs and various blood-pumping mechanisms during cardiac by-pass in dogs, but lungs of various species perfused with heterologous blood developed acute congestion with massive pulmonary edema.[4]

Mustard and associates[5] operated upon seven infants with transposition of great vessels using the Cowan Perfusion Pump and a biologic oxygenator (monkey lungs). Since their paper was primarily one of surgical approach for transposition of the great vessels, the technique for perfusion of human blood through the monkey lungs was not given, and no measurements of blood flow through the monkey lungs or pulmonary artery perfusion pressure in the monkey lungs were included in their article.

In our preliminary studies we used isolated autologous and homologous lung lobes for maintenance of respiratory function during thirty minutes of cardiac inflow occlusion and by-pass in dogs. Whereas the dogs were in good condition (that is, normal blood pressure, normal electrocardiogram, adequate spontaneous respiration) immediately after the by-pass, within a few hours virtually all of the dogs bled to death (with normal bleeding and clotting time, adequate platelets, and normal prothrombin time). Later the extracorporeal circuit was made completely of plastic, with the exception of the rubber tubing in the pump head and depulsator, and no hemorrhagic tendencies were noted in any of the next 20 dogs.[6] Subsequently all plastic dispersion type artificial oxygenators have been constructed in the department, and no postcardiac by-pass hemorrhages have been noted in dogs maintained on these all-plastic oxygenators.[7, 8]

The purpose of this paper is to describe in detail the technique of utilizing a heterologous lung oxygenator in human beings, but not to discuss direct-vision intracardiac correction of the defects encountered.

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This investigation was supported by a Research Grant (H-1784-C) from the National Heart Institute, of the National Institutes of Health, Public Health Service and the Graduate School, University of Minnesota.

Received for publication Aug. 24, 1955.

*Markle Scholar in Medical Sciences.

## METHODS

*Preparation of Heterologous Lung.*—A large, healthy mongrel dog is lightly anesthetized with intravenous Pentothal sodium (20 mg. per kilogram of body weight). Subsequently, heparin (2 to 3 mg. per kilogram) is given intravenously followed in a few moments by a second and lethal dose of intravenous Pentothal sodium. The right chest of the dog is clipped and shaved and removal of the lungs is carried out under aseptic conditions. The fourth or fifth intercostal space on the right is entered and two ribs above and below this level may be divided in order to obtain better exposure. The pulmonary ligaments are divided and the vena cavae, azygos vein, brachiocephalic arteries, and aorta are divided between clamps or ligatures. The pericardial sac is detached from the diphragm and the trachea is dissected from the esophagus. After freeing up the heart

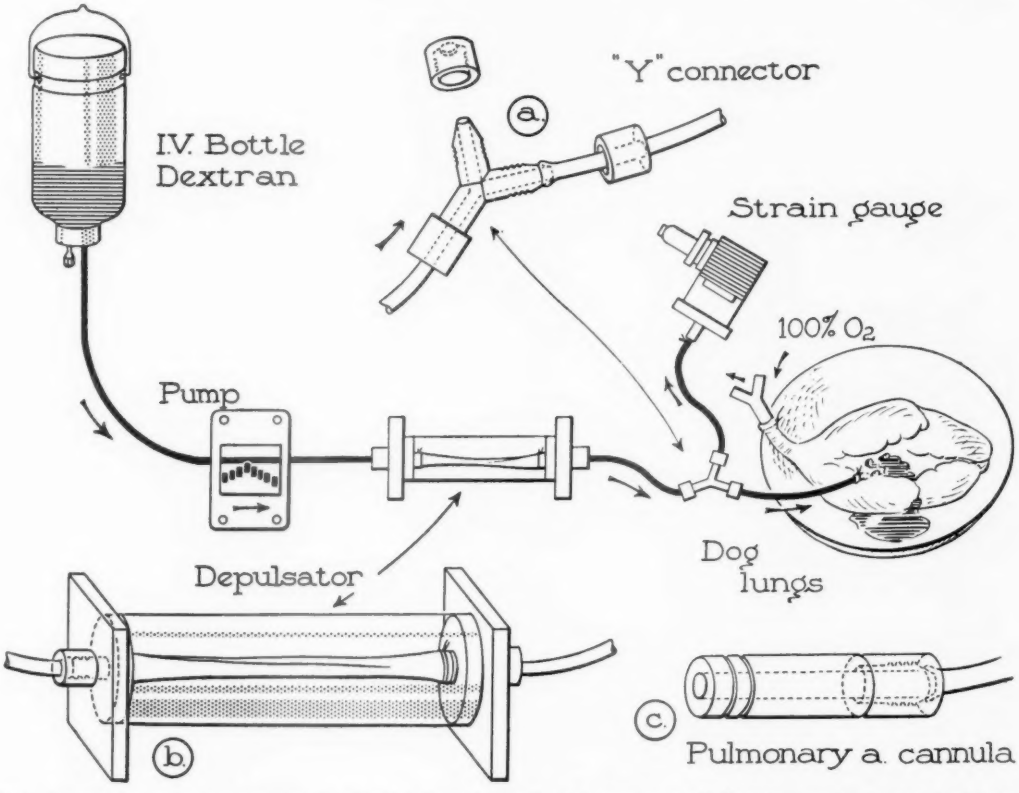


Fig. 1.—Technique for perfusion of dextran through the pump and depulsator into the isolated dog lungs.

and lungs, the trachea is divided high in the apex of the chest and the divided, Kocher-clamped trachea is considered contaminated. The heart and lungs are then placed in a sterile basin and the main pulmonary artery is dissected free and clamped at its origin from the right ventricle. Care is taken to avoid the entrance of air into the pulmonary artery. A plastic cannula (Fig. 1) with an attached piece of plastic tubing* (3/16 inch internal diameter with a 1/16 inch wall thickness) is inserted into the main pulmonary artery and the cannula is tied in place with two separate heavy silk ligatures which are seated into the grooves near the tip of the plastic cannula. The plastic tubing has previously been filled with warm (37° C.), 6 per cent dextran† and the tubing clamped in order to prevent the aspiration of air into the pulmonary arterial system. The pulmonary

*Mayon Plastics, 718 Washington Avenue North, Minneapolis, Minn.

†A generous supply of dextran (Plavolex) was donated by the Wyeth Laboratories of Philadelphia, Pa.

veins are identified at their entrance into the left atrium, and the left atrium is opened and excised in such a fashion as to leave a cuff of atrial tissue around each pulmonary vein. The pulmonary veins are not cannulated and, consequently, it is impossible to develop a back pressure on the pulmonary vascular bed. The noncannulization of the pulmonary veins is an added safeguard against the development of pulmonary edema.[6] The trachea is cannulated with a large-bore cannula, and the lung is partially inflated and the tracheal tube clamped in order to prevent atelectasis. Subsequently 1,500 to 2,000 c.c. of 6 per cent dextran is perfused through the isolated dog lungs at a monitored pulmonary

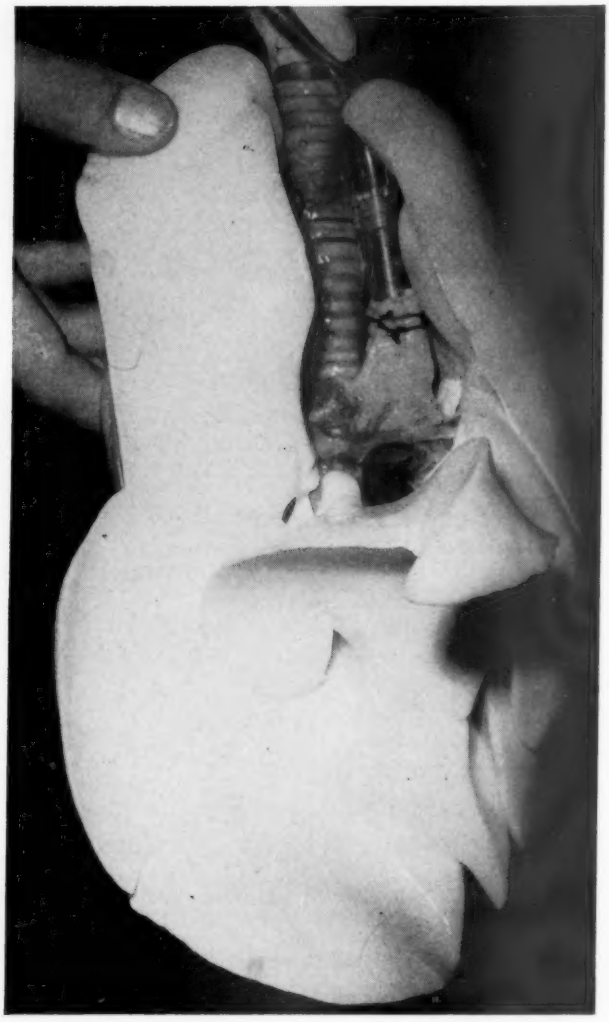

Fig. 2.—Appearance of dog lungs following removal of heparinized dog blood with dextran perfusion.

artery pressure as shown in Fig. 1. During the dextran perfusion the lungs are ventilated with air at an intermittent positive pressure of 12 to 18 cm. of water. This dextran is not recirculated through the lungs and, as more and more dextran is perfused through the lungs, the lungs become chalk-white in color (Fig. 2). Naturally, the dependent lobes are preferentially perfused and by tilting and/or rotating the lungs, the apical lobes are made dependent and are subsequently cleared of the heparinized dog blood. The lungs must be rid of the dog blood so that subsequent perfusion of these lungs with human blood

will proceed smoothly without the development of edema and congestion in the heterologous lungs. Saline solution and glucose should not be used to "wash out" the dog lungs since these solutions have no colloidal osmotic pressure and will readily pass across the capillary membrane and into the lung tissue. Initially, we used type specific dog plasma followed by type specific human plasma for cleansing the pulmonary vascular system of the lungs, but during the past seven months dextran has been used with excellent results. The flow rate of the dextran perfusion is approximately 200 to 400 c.c. per minute at a pulmonary artery perfusion pressure of 12 to 20 mm. Hg.

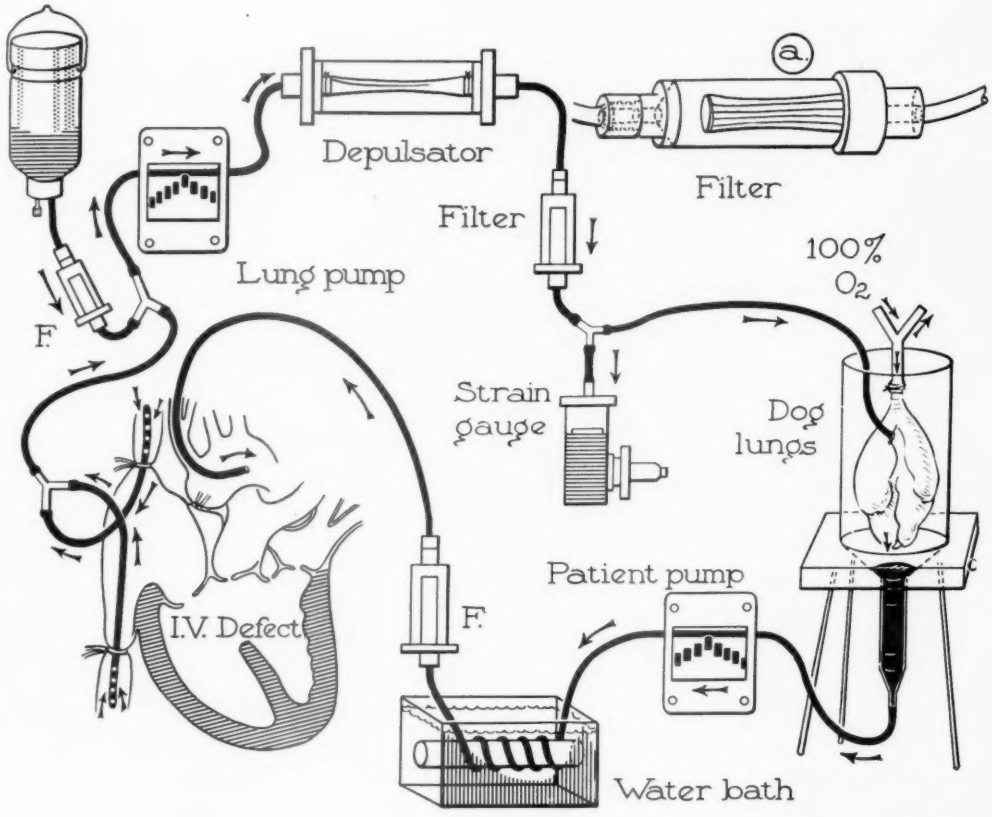


Fig. 3.—Extracorporeal cardiorespiratory circuit. The patient's blood is aspirated from the superior and inferior vena cavae, circulates through the extracorporeal circuit as illustrated by the directions of the arrows, and is returned to the right subclavian artery of the patient.

The depulsator (Fig. 1) between the pump and the lungs protects the lungs from high ejection (systolic) pressures which are noted with this relatively rigid plastic tubing when the depulsator is removed. The depulsator consists of a piece of sterile Penrose tubing 8 inches long and ⅝ inch in diameter interspaced between the plastic tubing and housed in a water-tight methyl methacrylate case.

*Extracorporeal Circuit.*—This circuit is diagrammed in Fig. 3. The lungs are removed from the dextran circuit by dividing the plastic tubing proximal to the pulmonary cannula and the lungs are placed in the methyl methacrylate chamber. The extracorporeal circuit is filled from a bottle of warm (37° C.), fresh, heparinized blood (15 to 20 mg. of heparin per 500 c.c.) on the accessory venous pick-up limb of the circuit. After the lung limb of the circuit has been filled, including the limb to the strain gauge which is used to record pulmonary artery perfusion pressures, the lung pump is kept running in order partially to fill the plastic lung chamber with blood. The lung pump is then stopped and the

lung tubing is coupled (Fig. 3) to the short length of plastic tubing leading into the pulmonary artery of the heterologous lungs. Subsequently, the patient pump is set in motion and blood is forced through the entire limb of the circuit, special care being taken to avoid trapping any air bubbles in this limb since this is the limb leading to the subclavian artery of the patient. Approximately 400 to 500 c.c. of blood is required to fill the extracorporeal circuit depending upon the length of plastic tubing used and the amount of blood pooled in the lung chamber. Attention is called to the plastic Y connectors and to the filters* housed in the methyl methacrylate chambers (Fig. 3).

*Ventilation of Heterologous Lungs.*—The lungs are ventilated with 100 per cent oxygen at an intermittent positive pressure of 12 to 18 cm. of water at a rate of 12 to 14 per minute. The expiratory side of our respirator has a large (¾ inch) solonoid valve which allows rapid, spontaneous deflation of the lungs. The tubing between the respirator and the tracheal cannula of the lungs is corrugated breathing hose, in this way kinking is avoided.

*The Pumps.*†—The pumps used in the dextran wash-out and in extracorporeal circuits are sturdy and reliable and have an explosion proof ¼ hp. motor. The pump will deliver constant flow even with resistance changes of 40 to 200 mm. Hg pressure on the outflow side. Latex rubber tubing (½ inch internal diameter and 9 inches in length) is placed in the pump head, and, obviously, the larger the tubing through the pump head the greater the flow at a given pump speed. With ½ inch tubing the pump delivers up to 1,600 c.c. of blood per minute. In the laboratory and in the operating room hemolysis has been minimal (10 to 36 mg. per cent).

*Cannulation of Patient.*—Two separate thin-walled plastic catheters (12 Fr. to 16 Fr. size, depending upon the size of the patient) are inserted through separate stab wounds in the right atrium and are positioned in the superior and inferior vena cava (Fig. 3). The catheters are held in place with purse-string sutures in the right auricular wall and are connected via a Y tube to the pick-up limb of the extracorporeal circuit. The patient's subclavian artery is cannulated with a catheter of similar size and the catheter is attached to the outflow limb of the extracorporeal circuit.

*Partial and Total By-pass of the Patient's Heart.*—The isolated lung is inflated with 100 per cent oxygen under controlled positive pressure and the respirator controls are set at the desired levels (usually an intermittent positive pressure 12 to 18 cm. of water at a rate of 12 to 14 per minute). The lung and patient pumps are turned on simultaneously, and the flow is increased to the desired level while the pumps are balanced against each other. Equation of venous aspiration from the patient, with intra-arterial return to the patient, is readily attained by observing the blood level in the plastic lung chamber. If the blood level rises it is obvious that blood is being aspirated from the patient more rapidly than it is being returned to the patient and the patient pump is speeded up and/or the lung pump is slowed. The lung pump would be speeded up and/or the patient pump slowed if the blood level were to fall. After the lung circuit and patient circuits have been balanced, a transient blood level fall in the lung chamber is probably due to interference with venous pick-up from the patient and this is corrected by preferential aspiration from the accessory venous reservoir which is held several inches below the patient's caval level. Ordinarily, it is necessary to admit little if any blood via the accessory venous pick-up route, but we feel that it is an important safety factor. The blood in this accessory reservoir is fresh, warm, heparinized blood since cold blood increases the pulmonary artery pressure in the isolated lung and decalcified citrated blood is contraindicated intra-arterially because of its detrimental cardiac effects.

The careful monotoring of the blood level in the lung chamber requires the constant vigilance of one individual. Once the desired flow and balance of flow are obtained (requiring one to three minutes), the cavae are occluded and the total cardiac by-pass is

*Baxter N-97 expendable plastic filter.
†Sigmamotor Model T-6S, 3 North Main, Middleport, N. Y.

begun. The pulmonary artery pressure in the heterologous lung is always monitored during the by-pass and if this pressure can be held below 25 mm. Hg, no edema or congestion of the heterologous lungs develop.

*Completion of Cardiac By-pass.*—The by-pass is not terminated abruptly, but the change from a total to a partial by-pass is made as the tapes on the cavae are loosened. If the heart dilates rapidly and the heart action becomes weak the tapes are snugged down and released more gradually. After the patient's heart action is good and the patient's lungs are well aerated, the pumps are turned off and the by-pass is terminated. The caval and subclavian catheters are then withdrawn.

*Coronary Sinus and Thebesian Vein Blood Loss During the Cardiotomy.*—No attempt is made to utilize the blood (usually 600 to 1,200 c.c.) aspirated from the heart during the cardiotomy. This blood is collected in a graduated cylinder coated with Antifoam and this blood loss is concomitantly and quantitatively replaced with banked blood through a polyethylene catheter in the patient's saphenous vein. Recently, we have quantitatively replaced the cardiotomy blood loss with warm, heparinized blood via the accessory venous pick-up limb. This can be done quite easily by elevating the venous reservoir bottles above the level of the patient. When this is done blood is preferentially aspirated from the venous reservoir rather than from the patient, and blood is transfused intra-arterially as fully oxygenated blood.

## RESULTS

*Laboratory Studies.*—Human blood can be perfused through the lungs of the dog employing the technique described herein: (a) dextran perfusion to remove heparinized dog blood; (b) open, noncannulated pulmonary veins; (c) depulsated pulmonary artery; (d) care as to ventilation of the isolated heterologous lung. However, whereas the dog lungs in vivo will tolerate a blood flow of several liters per minute at a normal pulmonary artery pressure, the isolated lungs of the dog will accept a flow of only 400 to 800 c.c. of either autologous blood, homologous blood, or heterologous (human) blood at the same pulmonary artery pressure. We are now investigating ways of increasing the flow by negative pressure ventilation of the lungs, positional changes of the lungs, and so forth. Citrated banked human blood has been perfused through the isolated lungs of a dog for 30 to 150 minutes without any evidence of pulmonary edema. This blood has subsequently been re-collected under aseptic conditions and bacteriologic studies have revealed no contamination. Subsequently, such blood was transfused into anemic terminal cancer patients with no immediate or delayed reactions, and one patient was subjected to a partial by-pass with this technique at a flow rate of 400 to 450 c.c. per minute for twelve minutes. Approximately two months later the partially by-passed patient was skin-tested with dog plasma (0.2 c.c. of 1:100 dilution) and the skin tests were negative. On the basis of these findings we felt justified in using this method of cardiorespiratory maintenance during total cardiac by-pass for direct-vision intracardiac procedures.

*Clinical Studies.*—Seven patients have been maintained with this pump-heterologous lung oxygenator during intracardiac surgery.* These patients weighed from 15 to 58 kilograms, the by-pass flows varied from 350 to 1,000 c.c. per minute, and the duration of the cardiac by-pass was from fifteen to forty-nine minutes. One patient (a 55 kilogram man with traumatic inter-

*Surgery was performed by Drs. C. W. Lillehei and R. L. Varco.

ventricular septal defects) is the only long-term survivor and another patient (a 46 kilogram woman with tetralogy of Fallot) died on the fourth postoperative day with outflow obstruction of the right ventricle. Three patients died on the operating table shortly after the following intracardiac procedures: (1) attempted correction of mitral insufficiency; (2) closure of interatrial and interventricular septal defects in a patient with corrected transposition of the great vessels; (3) excision of left ventricular aneurysm. Two patients died several hours postoperatively: one with a persistent interventricular defect following attempted correction of tetralogy of Fallot, and the second with right ventricular failure following closure of a ventricular septal defect in a patient with severe pulmonary hypertension. The by-pass technique as such worked well in all seven patients. In patients requiring a by-pass flow of 1,000 c.c. per minute, lungs from two dogs were arranged in parallel and the pulmonary artery perfusion pressure of each lung was monitored. Blood samples were drawn at the end of the by-pass period and the average oxygen content in the blood on the arterialized limb of the circuit was 21 volumes per cent whereas the blood in the venous limb of the circuit had an oxygen content of 9 volumes per cent.

Bleeding and clotting times were normal at the end of the by-pass and platelet counts ranged from 92,000 to 166,000.

## DISCUSSION

We feel that this technique is an effective, safe, and reliable means for cardiorespiratory maintenance during intracardiac surgery. There has been no problem with air emboli, hemorrhages, or allergic phenomena in any of the cases. In the clinical cases the isolated dog lungs showed varying degrees of pulmonary edema and congestion. The amount of edema varied directly with the level of the pulmonary artery perfusion pressure. In those cases requiring a low by-pass flow, edema in the heterologous lungs was absent or minimal, whereas the edema was moderate or marked in lungs subjected to a high flow at a high pulmonary artery pressure (greater than 40 mm. Hg). The lungs were weighed before and after the by-pass, and any weight gain in the isolated lungs was added to the operative blood loss.

Although the pump-heterologous lung works well as a means of short-term cardiorespiratory maintenance during intracardiac surgery, the long-term support to either a failing heart or a failing lung will probably ultimately be performed with the somewhat more complicated mechanical heart-lung apparatus of Gibbon[9] or Dennis.[10]

Glass seems to have a detrimental effect on the blood clotting mechanism as evidenced by the fact that in our earlier laboratory experiments with a partial glass circuit all the dogs bled to death postoperatively, whereas with an all-plastic system none showed any hemorrhagic tendency.

On the basis of our results we feel justified in utilizing this technique for somewhat less hopeless congenital cardiac patients. We believe that current

studies from this and other laboratories will lead to certain refinements in technique which will make much higher blood flows possible, at normal pulmonary artery pressure.

## SUMMARY

The development of pulmonary edema and congestion has been reported when an isolated lung is perfused with heterologous blood. In this study human blood has been perfused through isolated heterologous lungs (dog lungs) without the development of pulmonary edema; and the edema is prevented by: (a) dextran perfusion to remove heparinized dog blood, (b) open, noncannulated pulmonary veins, (c) depulsated pulmonary artery, (d) care as to ventilation of the isolated heterologous lung.

Seven patients have been subjected to intracardiac surgery while their cardiorespiratory function was maintained via the pump-biologic oxygenator described herein. Laboratory and clinical experiences with this method are described.

## REFERENCES

1. Sugarman, H. J., Wesolowski, S. A., Anzola, J., and Welch, C. S.: The Use of an Isolated Homologous Lung as a Donor Oxygenator, Bull. New England M. Center **13**: 107, 1951.
2. Mustard, W. T., and Chute, A. L.: Experimental Intracardiac Surgery With Extracorporeal Circulation, SURGERY **30**: 684, 1951.
3. Potts, W. J., Riker, W. L., DeBord, R., and Andrews, C. E.: Maintenance of Life by Homologous Lungs and Mechanical Circulation, SURGERY **31**: 161, 1952.
4. Wesolowski, S. A., Fisher, J. H., and Welch, C. S.: Heart Lung By-pass Using Pumps and Isolated Homologous Lungs, Surg., Gynec. & Obst. **95**: 762, 1952.
5. Mustard, W. T., Chute, A. L., Keith, J. D., Sirek, A., Rowe, R. D., and Vlad, P.: A Surgical Approach to Transposition of the Great Vessels With Extracorporeal Circuit, SURGERY **36**: 39, 1954.
6. Campbell, G. S., Crisp, N. W., and Brown, E. B., Jr.: Maintenance of Respiratory Function With Isolated Lung Lobes During Cardiac Inflow Occlusion, Proc. Soc. Exper. Biol. & Med. **88**: 390, 1955.
7. Shumway, N. E., and Lewis, F. J.: Personal communication.
8. DeWall, R., and Lillehei, C. W.: Personal communication.
9. Gibbon, J. H., Jr.: Application of a Mechanical Heart and Lung Apparatus to Cardiac Surgery, Minnesota Med. **37**: 171, 1954.
10. Newman, M. H., Stuckey, J. H., Levowitz, B. S., Young, L. A., Dennis, C., Fries, C., Gorayeb, E. J., Zuhdi, M., Karlson, K. E., Adler, S., and Gleidman, M.: Complete and Partial Perfusion of Animal and Human Subjects With the Pump Oxygenator, SURGERY **38**: 30, 1955.

## ADDENDUM

Since the submission of this report, 5 more patients with ventricular septal defects have been operated upon utilizing the pump-oxygenator described herein for cardiorespiratory maintenance. There are 3 long-term survivors in this group.

# CANCER OF THE BREAST IN INDIAN WOMEN

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ACCURATE vital statistics are not available in our country to assess the exact number of annual deaths due to cancer of the breast in women. However, our information is based on the reliable statistical reports of some of the main hospitals in this country, together with the data of our own cases at the Tata Memorial Hospital. From a scrutiny of this material we can endorse the view that cancer is as common a disease in India as in the West.

The object of this paper is to note the frequency with which cancer affects the breast and the other organs, and to record the incidence of this disease among the various communities, its clinical and pathologic manifestations, and the line of treatment adopted at our hospital with the five-year end result.

During a period of five years (1941-1945) 508 women were registered at the Tata Memorial Hospital suffering from breast cancer. Individual case reports of these patients were carefully analyzed, and from these studies we were able to obtain the following information.

*Incidence.*—Of all cancers in both sexes, cancer of the breast in women constituted 7 per cent. Considering cancer in women alone, the disease was noted in the breast in 20 per cent; in the genital organs in 40 per cent, and in other sites in the remaining 40 per cent. Pack and Livingston[1] found the incidence of cancer of the breast to be 10 per cent of all cancers. Dorn, as quoted by Ackerman and Del Regato,[2] placed the incidence of this disease in women alone as high as 26 per cent.

*Communities.*—Among the four communities in western India, namely, Hindus, Muslims, Indian Christians, and Parsis, a striking preponderance of the disease has been noted in Parsi women. The Hindu and Muslim women were found to have this disease to the same extent, whereas the Indian Christians had a trifle higher incidence. In Parsi women the frequency of this particular disease was three times that in Hindus or Muslims. The high frequency was not just accidental and was thoroughly scrutinized and found to be real. The entire Parsi community does not comprise more than 100,000 persons. Parsis as a rule do not marry as early as do Hindus or Muslims and marriage outside their own communal fold is very infrequent. Explanations offered for the high incidence of breast cancer are indefinite and not conclusive. Could it be that the late marriage resulting in delayed or scanty lactation leads to retention of breast secretions and ultimate production of a cancer, or that a sort of susceptibility is produced by marriages strictly restricted to the small community, or is there still an unknown inherent factor? We have records of

Received for publication Aug. 22, 1955.

several Parsi families in which three or even four intimately related members have suffered from cancer of the breast. Strangely enough, cancer of the genitalia is very infrequent among the Parsi women and rare too is oral cancer in that entire community.

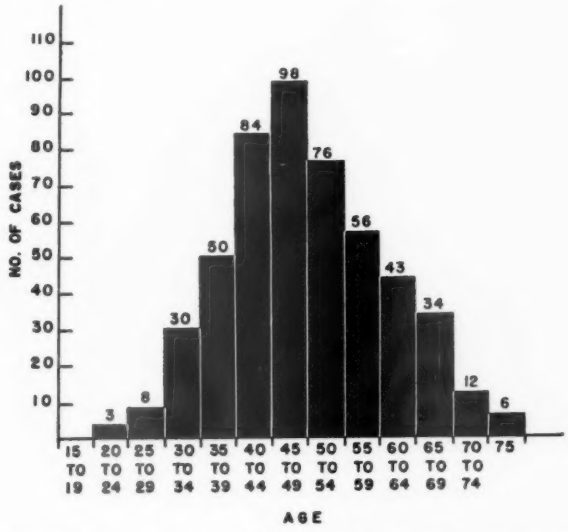


Fig. 1.—Age distribution of cancer of breast in Indian women, 500 cases.

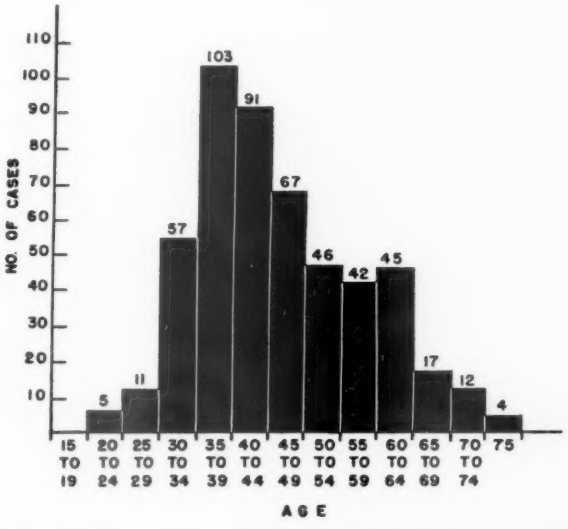


Fig. 2.—Age distribution of cancer of cervix in Indian women, 500 cases.

*Age.*—Until recently a false impression was prevalent that all cancers in Indian women occurred at an early age. The problem was studied and this wrong impression rectified. In our series, the highest incidence of cancer of the breast was observed in the age group of 45 to 49 years (Fig. 1), the same as in Western countries. In contrast, cancer of the cervix occurred in maximum number in the age group of 35 to 39 years (Fig. 2), ten years earlier than in Western women. The age group for cancer in other sites in women was noted

to be 45 to 49 years or older. The youngest person suffering from cancer of the breast was 21 years of age and the oldest was a woman of 83. Mammary cancer is rarely seen in women under 30 years of age. Occasional cases are recorded in very young persons.

*Predisposing Factors, Clinical and Pathologic Features.*—History of trauma to the breast before the lump was discovered was known in 6 per cent of our patients. Nine per cent suffered from chronic mastitis before cancer developed. Eighty per cent of our patients gave a history of a swelling or lump in the breast, the duration of which before a doctor was consulted varied from three days to three years. Serosanguineous or brownish discharge from the nipple was noted as the first symptom in 3 per cent of the patients. The average time lost before proper medical relief was sought has been calculated to be eleven months. The disease affected with about equal frequency the right and left breasts. The outer quadrants were more often affected than the medial ones.

The following clinicopathologic varieties were noted:

A. *Infiltrating or scirrhous carcinoma of the breast:* This was the commonest type. The classical textbook signs of cancer such as an indefinite, hard, painless lump producing retraction of the nipple and dimpling of the skin over the swelling are seen in this variety. As the disease progresses, fungation of the tumor occurs and large metastatic nodes develop in the axilla. In our series of 508 cases fungation of the tumor was present in 162.

B. *Circumscribed or localized form of adenocarcinoma:* A small per cent (10 per cent) of cancers were seen in this form. These tumors are of low-grade malignancy; they have a tendency to protrude from the surface of the breast; there may be cystic areas in the mass. The skin is often stretched but not adherent. Histologically, they are either papillary adenocarcinoma or adenocarcinoma which had undergone mucoid degeneration (gelatinous cancer) or comedocarcinoma.

C. *Paget's disease of the nipple:* This is an eczematous condition of the nipple associated with deep-seated cancer of the breast. We have three such cases in our series.

D. *Inflammatory or acute carcinoma:* In this variety a rapidly spreading area of inflamed skin appears over the breast early in the disease, and usually precedes the discovery of the underlying cancer mass. The dermal spread is caused by retrograde extension of the cancer cells through the lymphatics of the skin. Often, such patients are known to have fever, pain, leukocytosis, and enlargement of axillary lymph nodes. We had two cases of this type in the first five years.

E. *Cancer associated with pregnancy or lactation:* This is characterized by a rapidly growing mass in the breast which is painful and warm to the touch, and is accompanied by fever and leukocytosis. Axillary lymph nodes may or may not be enlarged. There were four cases of this type.

Fig. 3.—Scirrhous carcinoma of breast in an Indian woman.

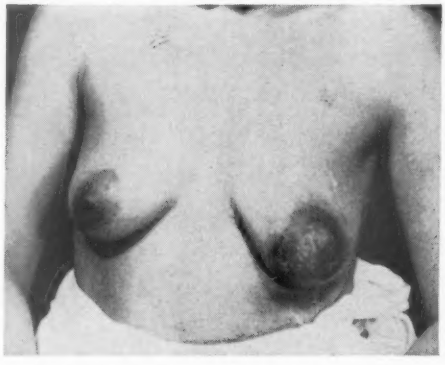

Fig. 4.—Paget's disease of the nipple in an Indian woman.

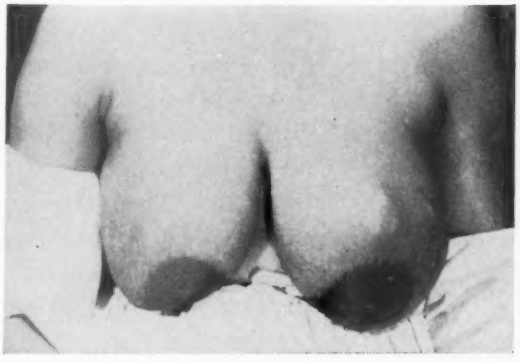

Fig. 5.—Circumscribed form of adenocarcinoma of the breast in an Indian woman.

We followed Steinthal's classification for the purpose of recording the stage of the disease:

| | | |
|---|---|---|
| Steinthal Stage I | 36 cases | 7.0 per cent |
| Steinthal Stage II | 172 cases | 33.7 per cent |
| Steinthal Stage III | 300 cases | 59.3 per cent |

It is obvious from these figures that a large number of patients came to us very late. The diagnosis in them was quite evident. An early cancer of the breast presents itself as a tiny, painless, movable lump, at which stage it is difficult to guess its nature. Here, a frozen-section pathologic examination is necessary. Such a procedure helped us to prove the presence of cancer on forty-five occasions and during the five years under review we were able to rule out cancer in almost fifty patients.

## TREATMENT

Table I indicates that only 240 patients were accepted for treatment. Every patient who had a reasonable chance of cure was given the benefit of treatment by a radical mastectomy which was followed by a course of deep x-ray therapy to the axillary and supraclavicular regions if the dissected lymph nodes showed metastatic deposits of carcinoma on microscopic examination. Inasmuch as we had a large number of advanced cases to treat, our criteria for radical operation were less rigid than those suggested by Haagensen and Stout.[3] Advanced, fungating cancers were treated by simple mastectomy followed by roentgen irradiation to the breast and axilla. In some cases only roentgen therapy was possible.

TABLE I. DISTRIBUTION OF CASES

| | |
|---|---|
| Total number of patients registered in O.P.D. (1941 to 1945) | 508 cases |
| A) Patients previously treated elsewhere now come for—recurrence, local, remote, or both | 62 cases |
| B) Patients previously treated elsewhere who have no disease—come for opinion only | 53 cases |
| C) Primary cancer cases—come for opinion only | 70 cases |
| D) Primary cancer cases with advanced disease and remote metastases—not accepted for treatment | 94 cases |
| E) Primary cancer cases plus few cases from Group A who were accepted for treatment | 240 cases |

We have had no opportunity to use radium in primary operable breast cancer, but we have implanted radon seeds with benefit in local recurrences and advanced inoperable cancers. Of 240 cases only 150 could be subjected to a radical mastectomy; the rest had to be treated with simple mastectomy plus irradiation, or with irradiation alone. There were two postoperative deaths following radical mastectomy. The local recurrence rate in our series was 16 per cent. Postoperative edema of the arm was noted in nine women; four of them developed edema within one year of the operation, but in the remaining five the swelling started for the first time after an interval of four to five years. All our patients with cancer of the breast associated with pregnancy or lactation died within eighteen months in spite of radical operation

in two and simple mastectomy with irradiation in the other two. Two of three patients with Paget's disease of the nipple were alive and well after five years. Our follow-up at best was only 80 per cent and patients not followed until the end of five years were considered "lost" for tabulating the end results.

TABLE II. RESULT OF TREATED CASES ACCORDING TO THE STAGE

| STAGE | NUMBER OF CASES | NO CLINICAL EVIDENCE OF DISEASE AT THE END OF 5 YEARS | PERCENTAGE |
|---|---|---|---|
| Stage I | 25 | 18 | 72 |
| Stage II | 84 | 27 | 32 |
| *Stages I and II | 109 | 45 | 41-2 |
| Stage III | 131 | 10 | 7.5 |
| Stages I, II and III | 240 | 55 | 22.9 |

*Operable cases.

Through the hard work of the recently inaugurated Indian Cancer Society we now get more early cases of cancer of the breast.

## SUMMARY

1. In India, cancer of the breast in women formed 7 per cent of all cancers.

2. In women, breast cancer accounted for 20 per cent, and cancer of the genitalia, 40 per cent.

3. For reasons not yet known, the frequency of the disease is quite high among the Parsi women.

4. Maximum number of cases were recorded in the age group 45 to 49 years. In contrast, cancer of the cervix occurred in maximum number in the age group of 35 to 39 years, ten years earlier.

5. From the cases accepted for treatment, only 10 per cent were in the early stage. In these the five-year cure rate was 72 per cent.

## REFERENCES

1. Pack, G. T., and Livingston, E. M.: Treatment of Cancer and Allied Diseases, vol. I, page 689.
2. Ackerman, L. V., and Del Regato, J. A.: Cancer, St. Louis, The C. V. Mosby Company, p. 926.
3. Haagensen, C. D., and Stout, A. P.: Carcinoma of the Breast, Ann. Surg. **116:** 801, 1942; **118:** 1, 1943.
4. Adair, F. E.: Radiation Therapy of Cancer of the Breast in Treatment of Cancer and Allied Diseases, Pack and Livingston, vol. I, Chapt. XLVI.

# CARCINOMA OF THE TONGUE

## Treatment and Results Without Radical Surgery

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IN TWO former communications from here by Dr. W. L. Mattick and associates, an appraisal was made of the results of irradiation therapy in 101 cases of cancer of the gum and 82 cases of cancer of the floor of the mouth. This present report on 247 cases of cancer of the tongue, treated during approximately the same period, will continue such study of intraoral neoplasia seen at the Roswell Park Memorial Institute. It is hoped that the combined data thus obtained from these studies can be of help in adequately determining the relative merits and indication for radiation therapy in comparison to the more recent trend to radical surgery in the treatment of intraoral carcinoma.

This is a clinical study of 247 consecutive cases of carcinoma of the tongue, treated at the Roswell Park Memorial Institute from 1937 through 1944.

During these years, the tongue cancers, both the primary and the metastatic lesions, were treated with radiation. No radical surgery was done.

We cannot present this series as pure radiotherapeutic results because in eighteen cases, an excisional biopsy rather than a punch biopsy of the lesion was done. As soon as the histology confirmed the diagnosis of carcinoma, however, these cases received a full course of radiation therapy.

The excisional biopsies were done on the smaller lesions (less than 2 cm. in diameter) limited to the mobile portion of the tongue. We know from experience and from cases treated by some of the older surgeons that many small lesions treated only by local excision, with an endotherm knife, remained healed for many years. In view of this, it is difficult to evaluate what effect the local excision produced and what effect the radiation produced in the survival of these cases in our present series.

We are not presenting this series to detract from or argue against radical surgery. We wish, however, to present these figures as a base line which will represent our results prior to radical surgery.

During the eight-year period from 1937 through 1944, 270 cases of tongue cancer were seen at the Institute. Twenty-three patients were not treated. Some were delinquent after the first visit, some preferred treatment elsewhere. These cases were eliminated, leaving 247 cases for analysis.

### Frequency, Age, Sex, and Etiology

During the same period (1937 through 1944), a total of 15,344 cases of cancer of all bodily locations were seen at the Institute. Of this number, 1,268 (8.2 per cent) were diagnosed as intraoral cancer of which 270 (21.1 per cent) had cancer of the tongue.

Received for publication Sept. 16, 1955.

The majority of patients were in the middle or older age groups. The youngest patient was 28 years of age and the oldest 88 years of age. The greatest number of cases fell in the fifth to seventh decade, as seen in Fig. 1. The sex ratio was 79 per cent (196 men) to 21 per cent (51 women).

The usual etiologic factors commonly conspicuous in causing chronic glossitis, either singly or in various combinations, were recorded: tobacco, poor oral hygiene, leukoplakia, avitaminosis, history of syphilis and/or positive blood Wassermann. Eighteen and two-tenths per cent of the cases with tongue cancer had a positive serology on admission and were presumed to have had a syphilitic glossitis at some time prior to the development of the malignancy.

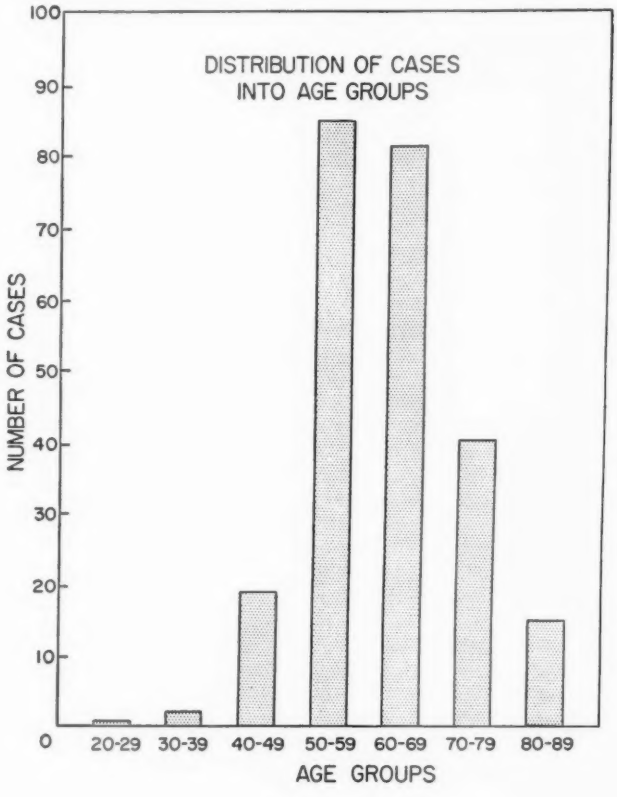


Fig. 1.

## DIAGNOSIS

Of all the lesions of the head and neck region, cancer of the tongue should ordinarily be fairly easy to diagnose. The history of a slow growing, generally painless ulcer is often characteristic. These lesions are either infiltrative or exophytic and are most commonly located on the mid-edge of the tongue. The alertness of the examiner, the indurative feel to palpation, and the result of punch biopsy generally make the final diagnosis.

Of major importance in prognosis and future management were such additional factors as: site of origin (oral portion or base of tongue), size of the

lesion, extent of induration, involvement of adjacent structures, character of the lesion (that is, infiltrative or exophytic) and the presence or absence of metastatic neck nodes. The grade of the tumor was also of some importance in management and prognosis. Complications, such as diabetes, alcoholism, and syphilis also reduced the prognosis and should be carefully noted.

## CLINICAL CLASSIFICATION

Many of the patients, when first seen, presented a rather advanced state, which often made it difficult to determine in just what area the lesion originated. The majority of lesions were located on the lateral edge of the tongue. In some cases, the entire tongue was involved and it was impossible to say whether the disease began on the dorsum of the tongue or whether there was extension from either one side or the other.

It has been our policy to describe the origin and the extent of the tumor, (that is, lesion involving the right middle third of the tongue with extension onto the floor of the mouth). In many cases, no attempt was made to measure the size of the lesion; first because of the technical difficulties involved and secondly because of the variation in the size of the oral cavities and tongues. A given-sized lesion may represent considerable involvement in one mouth, whereas, the same size lesion on a large tongue may be limited to the tongue only. In cases where more than one anatomic area of the tongue was involved, the area of greatest involvement was interpreted to be the site of origin.

For purposes of study, the tongue was divided into four anatomical areas. That portion anterior to the circumvallate papillae was referred to as the oral portion of the tongue and was divided into the anterior third, middle third, and posterior third. That portion behind the circumvallate papillae was called the base. All these lesions were then classified as right or left, although many of them extended well toward the midline and even beyond the midline in some cases. There were eight cases in which the entire tongue was involved and frozen in the floor of the mouth and these were grouped together.

All the lesions studied had histologic confirmatory diagnosis.

The nodal involvement on admission was clinically recorded and the results with and without nodes were analyzed.

## TREATMENT

All the cases included in this report were treated by some form of irradiation. In 18 patients, an excisional biopsy was done because the lesion was less than 2 cm. in diameter and it seemed more feasible to remove the entire lesion, (fifteen of these 18 patients lived longer than five years). These local excisions, however, were given immediate postoperative radiation therapy to the site because the excision was considered a biopsy and not a curative procedure.

Various forms of irradiation were used in the treatment of these lesions. In some cases, in which the tongue mass was infiltrative, interstitial radon seeds or radium needles were used. In some cases, especially when the growth was of the exophytic type, intraoral x-ray therapy was used.

The interstitial seeding was generally done in accordance with the Martin and Quimby tables using 1 mc. of radon (gold seed) with 0.3 mm. filtration. Radium needles when used, consisted of gold needles with 0.5 mm. platinum filtration, loaded with 2 mg. cells fastened to the tongue by linen sutures and left in situ for four days.

Intraoral x-ray therapy was given through lead cones, large enough to cover the lesion on the tongue and allow a centimeter of overlap onto normal mucosa. A 100 K.V. modality with 1 mm. Al. or with 0.9 mm. Cu. H.V.L. was used giving daily increments of 200 to 300 r. and carrying the total surface dose to approximately 6,000 r. Occasionally, a radium mold loaded with 2 mg. cells was applied. Here the dosage was 500 gamma r. daily for a total dose of 6,000 gamma r.

When the tongue was involved to a greater depth or when there were adjacent metastatic cervical nodes, the same 200 K.V.P. modality was applied through an external submaxillary field (8 by 10 or 10 by 15 cm.) directed to the tongue lesion and in some cases opposing parallel bilateral submaxillary ports, (8 by 10 or 10 by 15 cm. in size) directed at the tongue growth and including the nodes, were used. Treatments were given daily over a period of five to six weeks for a total surface dose of 6,000 r. In some cases, the 400 K.V. or 1,000 K.V. modality was used.

Under such therapy, the tongue and adjacent tissue showed evidence of mucositis. When external ports were used, the skin developed a weeping epidermolytic reaction. This generally resolved in two to three weeks following therapy. The tongue lesion generally regressed and often in the more favorable cases, completely disappeared. This was most frequently seen in the exophytic type of lesion.

Following treatment, the patients were reexamined every four to six weeks. If local recurrence or nodal metastasis was noted, further seeding of the growth or metastatic lesions was done. In some cases, further intraoral and/or external x-ray therapy, spotting the nodes, was given after an interval of six to eight weeks following the initial therapy.

## ANALYSIS OF TREATED CASES

There were 41 cases involving the lateral portion of the anterior third of the tongue. Thirty of these cases had no palpable nodes and 9 of these 30 lived more than five years, giving a 30 per cent five-year survival. Eleven cases had palpable nodes on admission and none lived more than five years. The over-all five-year survival for the 41 cases was 22.0 per cent.

There were 99 cases in which the lesion originated on the lateral mid-third of the tongue. Thirty-seven had clinically palpable nodes on admission and of these, none lived five years. Sixty-two cases had no nodes on admission and seventeen cases survived five years, giving a five-year survival of 27.4 per cent. The five-year over-all survival for all ninety-nine cases, however, was 17.1 per cent.

Lesions involving the lateral portion of the posterior third of the tongue totaled 58 cases. Twenty-seven cases had nodes and 2 of these survived over

five years, giving a survival of 7.4 per cent. Thirty-one cases had no nodes and 10 or 32.2 per cent survived more than five years. The survival for the entire 58 cases was 20.7 per cent.

The lesions originated in the right or left base in 41 cases. Thirty cases had nodes on admission and two or 6.6 per cent lived longer than five years. Eleven cases had no nodes on admission and two or 18.1 per cent lived more than five years. The survival for the entire group was 9.8 per cent.

In 8 of our cases, the entire tongue was involved. Strangely enough, two of these had no palpable nodes on admission. None lived five years. The longest survivor had palpable cervical nodes on admission and lived twenty-six months.

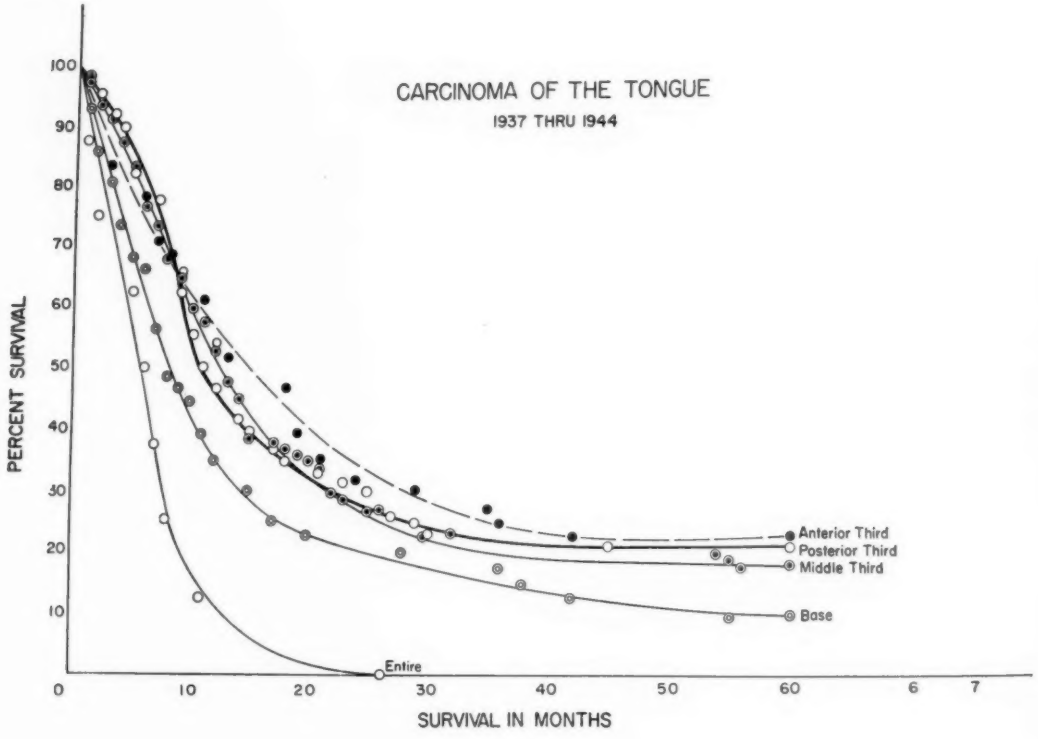


Fig. 2.

The portion of the tongue most frequently involved was the lateral edge of the middle third. We have summarized the above findings in Table I.

After studying these figures, we concluded that our absolute five-year survival for the oral portion of the tongue was 19.1 per cent but in those cases without nodes, the survival was 29.1 per cent. The absolute survival for the base of tongue lesions was 9.8 per cent, but again when only those cases without nodes were considered, the survival was considerably better (18 per cent.) The absolute five-year survival for all 247 cases was 17.0 per cent.

In an attempt to portray our survival figures more clearly, we graphed the per cent of cases against the survival in months. The survival curves in Fig. 2 graphically portray the results of all treated cases.

The curves for the anterior third, middle third, and posterior third of the tongue (oral portion or that portion anterior to the circumvallate papillae) were, for practical purposes, superimposed one on another. The base of the tongue showed the same general survival curve, but it fell well below the curves of the oral portion of the tongue.

It was noted from reading the curves that at the end of the first year, approximately 50 per cent of the patients with oral tongue lesions and 65 per cent of the patients with base lesions were dead. As a corollary to this, one may say that the prognosis improved considerably for those patients who survived the first year.

TABLE I. SUMMARY OF RESULTS, ROSWELL PARK MEMORIAL INSTITUTE, 1937 THROUGH 1944
(NO RADICAL SURGICAL PROCEDURES)

| | ALL CASES | | | WITH NODES | | | WITHOUT NODES | | |
|---|---|---|---|---|---|---|---|---|---|
| | NUMBER OF CASES | NUMBER OF FIVE-YEAR SURVIVALS | PER CENT OF SURVIVALS | NUMBER OF CASES | NUMBER OF FIVE-YEAR SURVIVALS | PER CENT OF SURVIVALS | NUMBER OF CASES | NUMBER OF FIVE-YEAR SURVIVALS | PER CENT OF SURVIVALS |
| Anterior one-third of the tongue | 41 | 9 | 22.0 | 11 | 0 | 0 | 30 | 9 | 30.0 |
| Middle one-third of the tongue | 99 | 17 | 17.1 | 37 | 0 | 0 | 62 | 17 | 27.4 |
| Posterior one-third of the tongue | 58 | 12 | 20.7 | 27 | 2 | 7.4 | 31 | 10 | 32.2 |
| Base | 41 | 4 | 9.8 | 30 | 2 | 6.6 | 11 | 2 | 18.1 |
| Entire tongue | 8 | 0 | 0 | 6 | 0 | 0 | 2 | 0 | 0 |
| Total | 247 | 42 | 17.0 | 111 | 4 | 3.6 | 136 | 38 | 28 |

## METASTATIC NODES

Forty-five per cent of our patients had clinically palpable metastatic nodes on admission. Several other patients subsequently developed nodes during the course of follow-up care. Martin and associates reported an incidence of 39 per cent clinically positive nodes on admission. Baud, 1948, reported that 56 per cent of her cases clinically had nodes on admission, and Jacobson reported an incidence of 48 per cent clinically positive nodes.

One hundred and thirty-six of our patients had no nodes on admission. Twenty-eight per cent of these lived for five years. One hundred and eleven patients had nodes on admission and 3.6 per cent lived five years. These figures indicated that radiation can hope to cure only an occasional case when the patient presents himself with clinically palpable metastases.

## BASE OF TONGUE

The cancers on the base of the tongue gave less favorable therapeutic results as compared with those on the oral tongue.

The lesions on the base of the tongue tended to be more anaplastic than those on the oral portion. Sixty per cent of the lesions on the base of the tongue

were of Grades I and II and 40 per cent were of Grades III and IV, whereas 82 per cent of the lesions on the oral tongue were Grades I and II, and 18 per cent were Grades III and IV.

This less differentiated grading of lesions of the base has generally been assumed accountable for the poorer prognosis in this location and seemed substantiated in this series.

## GRADING

The histologic slides were reviewed and the sections were graded, using Broder's criteria. The effect of anaplasia or differentiation on treatment was analyzed (Table II). Forty per cent of the 247 cases were of Grade I. Thirty-two per cent of the Grade I lesions had clinically metastatic nodes and the five-year survival was 20 per cent. Thirty-eight per cent were of Grade II, 52 per cent had nodes and the survival was 17 per cent. Sixteen per cent were of Grade III, 55 per cent had nodes and the survival was 13 per cent. Five per cent were of Grade IV, 54 per cent had nodes and the survival was 8 per cent.

TABLE II. GRADING (BRODER) AND ITS RELATIONSHIP TO NODAL INVOLVEMENT AND FIVE-YEAR SURVIVAL

| GRADE | PER CENT OF CASES | PER CENT WITH POSITIVE NODES | PER CENT OF FIVE-YEAR SURVIVAL |
|---|---|---|---|
| I | 40 | 32 | 20 |
| II | 38 | 52 | 17 |
| III | 16 | 55 | 13 |
| IV | 5 | 54 | 8 |

The survival rate was definitely better in lesions of Grade I and Grade II. The survival rate, however, appeared to be more closely related to the presence or absence of metastatic nodes at the time of treatment (Table I).

## CONCLUSIONS

Much of the relevant data has been summarized in Fig. 2 and Tables I and II, however, the more important points will be reviewed.

Table I clearly depicts the survival based on the presence or absence of presumedly metastatic nodes. Lesions on the oral portion of the tongue responded better than those on the base. The base lesions were often more anaplastic and had a poorer prognosis.

The effect of treatment on the primary tumor and the metastatic nodes as related to histopathologic grading was referred to in Table II. The Grade I and II tumors showed a better survival rate than the more anaplastic types which often, while quite immediately responsive to therapy, were, on the other hand, more prone to recurrence and dissemination.

Lesions which received excisional biopsy (lesions less than 2 cm. in diameter, limited to the mobile portion of the tongue) and immediate irradiation showed the best survival of all. Fifteen out of 18 cases or 80 per cent survived five years or longer, thus demonstrating the prognosis of the small lesions, and/or early therapy. In comparison, the eight cases in which the entire tongue was involved showed no five-year survivals.

In a few cases, where the primary lesion had remained healed for five or more years, delayed neck node metastases occurred. In another small number, without evident recurrence, a late radio osteonecrosis of the mandible occurred.

Of the 45 patients with a positive blood serology, only 8.9 per cent survived five years or more.

There were 42 five-year survivals and these cases were reviewed as a group. In 15 of the 42 cases, the lesion was less than 2 cm. in diameter. Thirty-nine or 93 per cent of the 42 cases had no clinically palpable nodes on admission. This group included 13 women (25 per cent of all the women in the series) and 29 men (15 per cent of all the men in the series). Although this difference was probably not statistically significant, the clinical impression was that women seemed to do somewhat better than men.

Cases were further assessed in Table III on the basis of determinate and indeterminate results as suggested by Martin, Berven, and others. Here, it will be noted that the determinate results from our clinic were slightly lower (16.2 per cent) than the exclusive radiation results of Bervan (21.3 per cent), while the absolute results were quite similar (15.4 per cent to 15.2 per cent). By comparison, Martin's determinate figure of 25 per cent may therefore be looked upon as representing the additional gain to be achieved by a more concerted surgical approach, including hemiglossectomy, neck dissection in addition to radiation. It is expected that the more radical surgical therapy adopted here since 1944 will also similarly improve survivals by an increment of approximately 10 per cent.

TABLE III. ROSWELL PARK MEMORIAL INSTITUTE (1937-1944)

| | | |
|---|---|---|
| Total Number of Patients | | 247 |
| Indeterminate Group | | |
| Dead of other causes without recurrence | 10 | |
| Lost Track of without recurrence | 2 | |
| Total Indeterminate | | 12 |
| Determinate Group (Total minus Indeterminate) | | 235 |
| Failures: | | |
| Dead as a result of cancer | 189 | |
| Lost Track of with disease | 4 | |
| Living with recurrence | 4 | |
| Total number of Failures | | 197 |
| Successful results: Free from disease after five years | | 38 |
| Five-year end results: Success Results 38 / Determinate Results 235 | | 16.2 per cent |

The more recent experience of our clinic makes it apparent that the more radical surgical approach (hemiglossectomy, hemimandibulectomy and neck dissection) is often necessary to improve the over-all end results of tongue cancer. Though radiation therapy has been known to cause the disappearance of metastatic neck nodes, experience has shown that radical neck dissection will produce better end results. Where bone is invaded, the radiation is of no avail. Here radical neck dissection en bloc with hemimandibulectomy should be practiced.

SUMMARY

1. Two hundred and forty-seven cases of carcinoma of the tongue treated almost exclusively by irradiation therapy were presented. No radical surgery was done.

2. The absolute five-year survival rate for all cases of tongue cancer was 17 per cent.

3. The absolute survival rate for lesions on the oral portion of the tongue was 19.2 per cent. In these cases without neck nodes, the survival rate was 29.3 per cent.

4. The absolute survival rate of lesions on the base of the tongue was 9.8 per cent.

5. Sixteen and two-tenths per cent of all cases were free of disease for five years or more. This figure was approximately 10 per cent lower than that of clinics where irradiations supplemented by radical surgery was practiced and thus demonstrated the advantage in degree for this later type of management.

6. Irradiation cured only an occasional case with cervical metastases.

7. The more differentiated lesions gave a higher survival rate than the less differentiated ones. The survival, however, was more closely related to the presence or absence of nodes at the time of treatment.

8. The smaller lesions without neck nodes and without bone invasion showed the best survival.

REFERENCES

1. Baud, J.: End Results of Radiotherapy of Cancer of the Tongue, Am. J. Roentgenol. 63: 701, 1950.
2. Berven, Elis: End Results of Treatment of Cancer of the Tongue, Am. J. Roentgenol. 63: 712-715, 1950.
3. Jacobsson, F.: Carcinoma of the Tongue, a Clinical Study of 277 Cases Treated at Radiumhemmet, 1931-1942. Acta radiol. Suppl. 68: 1-184, 1948.
4. Martin, H. E., Munster, H., and Sugarbaker, E. D.: Cancer of the Tongue, Arch. Surg. 41: 888, 1940.
5. Mattick, Walter L., and Meehan, Donald J., Carcinoma of the Gum, SURGERY 29: 249, 1951.
6. Mattick, Walter L., Meehan, Donald J., and Haberlin, John P.: Squamous Cell Carcinoma of the Floor of the Mouth, SURGERY 31: 575, 1952.

# THE MANAGEMENT OF ACUTE MASSIVE VENOUS OCCLUSION

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PHLEBITIS is a common disease with symptoms varying from the mild to the extremely severe. Acute massive venous occlusion, which is a very severe and dramatic form, was first described by Trémolières and Véran[11] in 1929. This entity has also been described by Gregoire[4] as "blue phlebitis" or phlegmasia cerulea dolens. The term "thrombophlebitis with ischemia and gangrene" has been employed by Hershey and Snyder[6] in conformity with the terminology used by Audier and Haimovici,[1] and Decoulx and Bastien.[3] We recommend acceptance of the term "acute massive venous occlusion" as suggested by Veal and associates[12] as the most fitting.

DeBakey and Ochsner,[2] in 1949, and Haimovici,[5] in 1950, reviewed the literature. The reported cases are few and the series are small; accordingly final conclusions are dangerous. It seems wise that divergent opinions be presented so that the logical and most efficacious therapy can be evolved. It is with this in mind that an additional three cases are summarized, with a concept of the therapy offered.

Usually the onset of acute massive venous occlusion is rapid and dramatic. Characteristically, there are rather severe pain, rapidly appearing edema, and a mottled, violaceous cyanosis from which the entity derives its name. In about two-thirds of these cases there is an absence of arterial pulsation in the area of involvement. The arrest of the process at various stages and degrees has been described. Haimovici[5] describes three phases, namely, phlegmasia alba dolens, which preceded phlegmasia cerulea dolens in 44 per cent; phlegmasia cerulea dolens as an initial manifestation in 56 per cent; and gangrene of venous origin which always has phlegmasia cerulea dolens apparent as part of the process.

The etiology is not yet clearly understood. The process has been known to follow surgery for various disorders, trauma, visceral malignancy, pulmonary disease, and cardiac disorders. In a few patients there is no known associated factor. In Veal's series,[12] cases followed ligation of the inferior vena cava, and femoral and external iliac veins. He attributes some cases to a proximal migration of venous thrombi. One of his cases followed chemical instillations at the time of saphenous vein ligation. Hershey and Snyder[6] had two of three cases appearing four and five days after the ligation of a superficial femoral vein.

Also the pathologic-physiologic background is not settled. DeBakey and Ochsner,[2] Hershey and Snyder[6] and Haimovici[5] attribute the process to a massive block of venous return and they feel that arterial and vasospasm contribute to the problem. Manheimer[8] suggests the role of massive venous occlusion

Received for publication Sept. 21, 1955.

also, but he believes the role of venous spasm is fundamental. Laufman and associates[7] found in venous occlusion a marked arterial spasm with venous dilation. Osius[10] agrees with the latter, suggesting that in partial obstruction one finds slowing, sludge formation, and thrombosis, while in complete obstruction there is venous thrombosis and ultimately arterial thrombi, anoxia, tissue asphyxia, and gangrene.

It would appear that massive interference in venous return is fundamental to the process. The extent and ramifications of the disease would depend upon the addition of arterial and venous spasm. The latter is exemplified in one of our cases. The patient progressed from thrombophlebitis to massive venous occlusion. She then had gangrene of venous origin and finally the total gangrene of arterial thrombosis. The gangrene of venous origin is usually superficial and accordingly suggests conservative therapy.

The treatment of acute massive venous occlusion has varied. Veal[12] recommended conservative treatment by high elevation and vigorous muscle action; Osius[10] suggested ligation of the superficial femoral vein after thrombectomy. Miles,[9] reporting one case, felt ligation of the inferior vena cava to be the superior method of therapy.

The strongest objection to the conservative method is the potential danger of an embolus from the dislodgement of a venous clot. The advantage of avoiding surgery in a very sick patient is evident, and it is justified only if it offers a more favorable outcome.

Thrombectomy offers a rapid and dramatic improvement in some patients. The reopening of significant venous channels following the removal of large clots would seem to more favorably alter the pathologic anatomy and, in addition, there is less likelihood of a major embolus. One cannot, however, avoid the paradox that the therapy offered also is listed as a possible etiology in some cases reported.

It is our opinion that in certain instances one can serve the patient best by early thrombectomy. One cannot ignore the progressive nature of the disease in some cases. The reopening of major channels should aid in halting the extension of the process and it may also reduce the incidence of late vascular insufficiency syndromes. Pulmonary embolization was present in two of our cases and this serves to emphasize the need of a vigorous approach in this group of patients.

The level of ligation should vary with the patient, and this is demonstrated in our group of cases. In Case 1, with repeated pulmonary emboli and massive involvement of the left leg with venous occlusion, it was felt the safest treatment was surgery. The inferior vena cava was ligated in continuity and the left superficial femoral vein was closed after thrombectomy was performed through it. The patient improved rapidly. If emboli enter into the problem, this combined approach is recommended. If the disease is limited to massive venous occlusion, we feel ligation of the superficial femoral vein after thrombectomy may be preferable. We would recommend that the entire leg be prepared and draped into the operative field so that the immediate effects of surgery become

apparent. In Case 2, we felt that the clot aspiration had not been entirely satisfactory but the leg was draped out of the field and the inadequacy was not fully appreciated until the wounds were closed. Further suction combined with vigorous muscle massage while the patient is under anesthesia could well enhance the extent of clot removal and the collateral blood flow. If this occasion should again arise, we would reopen the field and complete this program.

Postoperatively, the legs should be wrapped in elastic bandages, elevated acutely with the foot of the bed also raised, and active muscle action should be started. We have not employed anticoagulants postoperatively. At the present, we favor the surgical attack in most patients. If this is combined with the recommended postoperative management, the undesirable complications and late manifestations of the disease will be minimized.

CASE 1.—M. K. This 19-year-old boy had a right inguinal hernia repaired elsewhere on July 20, 1954. He was dismissed after an uneventful postoperative course on July 27. He was readmitted to the hospital on July 31 with the diagnosis of pulmonary infarct. Three days later he had a second embolus with severe pain and cyanosis. The left leg became tender and progressively passed through the typical phlegmasia alba dolens to an early phlegmasia cerulea dolens. He was treated by leg elevation, oxygen, and Depo-Heparin. He entered the B. C. H. on our service on August 9, acutely ill and complaining of severe chest and left leg pain. The left leg was very painful, tender, and acutely swollen to the groin with moderate cyanotic mottling. Pulsations were absent in this extremity. Chest roentgenogram revealed a right pulmonic infarct. He was treated with oxygen, morphine sedation, and leg elevation. On August 10, an inferior vena caval ligation below the renal veins was accomplished without difficulty. Immediately following this, the common femoral vein was exposed on the left. After vein control was obtained by umbilical tapes, large clots were removed from the iliac and superficial femoral veins. Free bleeding resulted both proximately and distally. The vein was closed with 5-0 arterial silk using everting sutures. The legs were wrapped in elastic bandages, acutely elevated with the foot of the bed also elevated, and active muscle action was started. The postoperative course was entirely benign and the wounds healed primarily. The right leg, on ambulation, caused some pain and tended to swell more than the left. Both were well controlled by elastic supportive dressings. He was dismissed from the hospital on the fourteenth postoperative day in good condition and has remained well since then.

CASE 2.—Patient W. S., age 49, was admitted to B. C. H. on Oct. 24, 1954. She had right pleuritic pain, a low grade temperature, and slight tenderness in the right calf. Chest roentgenogram revealed a pulmonic infarct. Past history was negative except for a recent mild pulmonary infection. Management with Dicumarol brought about steady improvement. She was dismissed to her home on November 5. She did well until December 23 when severe leg pain awakened her from sleep. There was severe pain and tenderness with mottled cyanosis of the left foot, leg, and thigh. Arterial pulsations were absent on the left but she could move the toes. It was elected to do a vena caval ligation. She was operated upon on December 23 with ligation in continuity of the inferior vena cava below the renals. The left superficial femoral vein was exposed, prepared and opened. A large amount of clot was aspirated both proximally and distally with free bleeding resulting. The vein was then ligated. Her convalescence was slowed by ileus but otherwise was not remarkable. She was ambulatory on the seventh postoperative day and the leg swelling was well controlled by elastic bandages. She was to be dismissed on Jan. 2, 1955, when she again had a sudden onset of severe pain, swelling and mottled cyanosis involving the opposite foot, leg, and thigh. Again there was no palpable arterial pulsation in the involved area and no paralysis. She was returned to surgery and the right superficial femoral vein was exposed, prepared, and opened. Large clots were aspirated from the proximal portion of the vein with resultant free bleeding. The clot extraction distally was only fairly successful and the bleeding much less vigorous. The vein was then ligated.

The right foot, leg and thigh remained cyanotic, cold, and painful although it was kept markedly elevated. On January 5 a continuous caudal anesthetic was instituted with relief of the severe pain but with no objective improvement. After three days this was discontinued. The skin of the right foot and toes became vesiculated and advanced to typical venous gangrene. Slowly the process increased and deep extensive gangrenous involvement from the ankle down ensued. On January 25, an amputation was performed below the knee. The pathologic specimen showed massive venous thrombosis, with thrombosis of the posterior tibial artery and gangrene of the foot and toes. Following amputation, the patient improved rapidly and was dismissed from the hospital on February 4. At that time the condition of the left lower extremity was satisfactory and the right leg stump was healing kindly. Since then she has done well and is ready for prosthesis fitting.

CASE 3.—L. K., age 46, was admitted to B. C. H. on July 19, 1954, complaining of pain in the right chest of two months' duration, pain in the right foot and ankle of two weeks' duration, and enlarged lymph nodes in the right supraclavicular space. Examination was essentially negative except for the enlarged supraclavicular nodes on the right. Rhonchi were present over both lung fields. There were slight swelling of the right lower leg and deep calf tenderness. Pulsations in both lower extremities were normal.

A chest roentgenogram was suggestive of a lesion of the left lower main stem bronchus. A biopsy of the lymph nodes on July 20 revealed metastatic carcinoma to the lymph nodes, the site not determinable. The patient was obviously deteriorating.

On August 4 she complained of severe pain in her left foot and leg. The extremity was swollen and cold, and showed mottled cyanosis. It was elected to treat the acute massive venous occlusion by elevation and Dicumarol in the face of the hopeless carcinoma. She required narcotics to control the severe pain. No noticeable improvement occurred at any time. On August 17 the right foot and leg became similarly involved, and two days later the toes and dorsal aspects of both feet showed beginning venous gangrene. This progressed slowly to involve a portion of each foot. The tissues of the toes went from a superficial loss of vitality to complete death. The patient died on Aug. 27, 1954.

## SUMMARY

1. The disease of acute massive venous occlusion is presented from an etiologic and pathologic basis.

2. A program of therapy is outlined.

3. Three cases of acute massive venous occlusion are reported.

## REFERENCES

1. Audier, M., and Haimovici, H.: Les gangrènes des membres d'origine veineuse, Presse méd. **2**: 1403-1406, 1938.
2. DeBakey, M., and Ochsner, Alton: Phlegmasia Cerulea Dolens and Gangrene Associated with Thrombophlebitis, SURGERY **26**: 16, 1949.
3. Decoulx, P., and Bastien, P.: Gangrène par spasme artériel au cours d'une phlébite, Ann. anat. path. **16**: 353, 1939.
4. Gregoire, R.: La phlébite bleue (phlegmatic caerulea dolens), Presse méd. **46**: 1313, 1938.
5. Haimovici, H.: Gangrene of the Extremities of Venous Origin, Circulation **1**: 225, 1950.
6. Hershey, C. D., and Snyder, Roy E.: Thrombophlebitis With Ischemia and Gangrene. SURGERY **34**: 296, 1953.
7. Laufman, H., Martin, W. B., and Tuell, S. W.: The Pattern of Vasospasm Following Acute Arterial and Venous Occlusions: Micrometric Study, Surg., Gynec. & Obst. **87**: 641, 1948.
8. Manheimer, Leon H., and Levin, Leo M.: Phlegmasia Cerulea Dolens, Angiology **5**: 472, 1954.
9. Miles, Robert M.: Phlegmasia Cerulea Dolens: Successful Treatment by Vena Cava Ligation, SURGERY **30**: 718, 1951.
10. Osius, Eugene A.: Acute Massive Venous Occlusions, Arch. Surg. **65**: 19, 1952.
11. Trémolières, F., and Véran, P.: Syndrome d'oblitération artérielle du membre inférieur droit apparu au cours d'une phlébite superficelle et profonde avec embolies pulmonaires. Effect thérapeutique de l'acétylcholine, Bull méd., Paris **43**: 1101, 1929.
12. Veal, J. Ross, Dugan, T. G., Jamison, Wm. L., and Bauersfeld, R. S.: Acute Massive Venous Occlusion of the Lower Extremities, SURGERY **29**: 355, 1951.

# A NEW SUTURE METHOD FOR LIVER RESECTION

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UNCONTROLLED bleeding is the greatest problem associated with resecting large segments of liver. A simple and adaptable liver suture technique was used successfully for hemostasis in three individuals in whom major portions of liver parenchyma were removed. The clinical data referable to these cases are summarized in Table I.

TABLE I.

| | K. S. (60-YEAR-OLD WHITE WOMAN) | M. W. (52-YEAR-OLD WHITE WOMAN) | W. S. (52-YEAR-OLD WHITE MAN) |
|---|---|---|---|
| Primary complaint | Nontender mass in right upper quadrant for 12 months | Tender mass in right upper quadrant for 1 month | Tender mass in right upper quadrant for 1 week |
| Amount of liver resected | Right lobe 65% | Right lobe 35% | Right lobe* 50% (16 by 11 by 9 cm.) |
| Blood replacement | 500 c.c. | 500 c.c. | 500 c.c. |
| Pathologic report | Hepatocellular carcinoma | Liver adenoma; no malignant areas seen | Hepatocellular carcinoma |
| Size of tumor mass | 12 by 15 by 11 cm. | 5 by 4 by 4 cm. | 5 by 4 by 4 cm. |
| Follow-up | 53 mo. postop. dead; recurrences in right scapula and abdomen | Living and well 47 mo. postop. | Living and well 6 mo. postop. |

*See Figs. 3 and 4.

Fig. 1, *A* to *G* illustrates the placement of the hemostatic "cobbler" type suture. The steps pertinent to its use are as follows.

## METHOD

The needle is formed by bending No. 16 silver wire 20 inches long upon itself so that an open narrow loop is formed. This loop acts as the needle point (Fig. 1, *A*).

The looped end of this wire needle is passed through the liver parenchyma near one margin 1 to 2 cm. proximal to the proposed line of resection (Fig. 1, *A*).

A full length of a No. 2 chromacized catgut suture† is then passed through the "eye" of the loop of wire and the wire is withdrawn, so that a loop of the catgut suture is brought through the liver (Fig. 1, *A* to *C*).

Received for publication Aug. 25, 1955.

*John and Mary Markle Scholar.

†Ribbon catgut may be used.

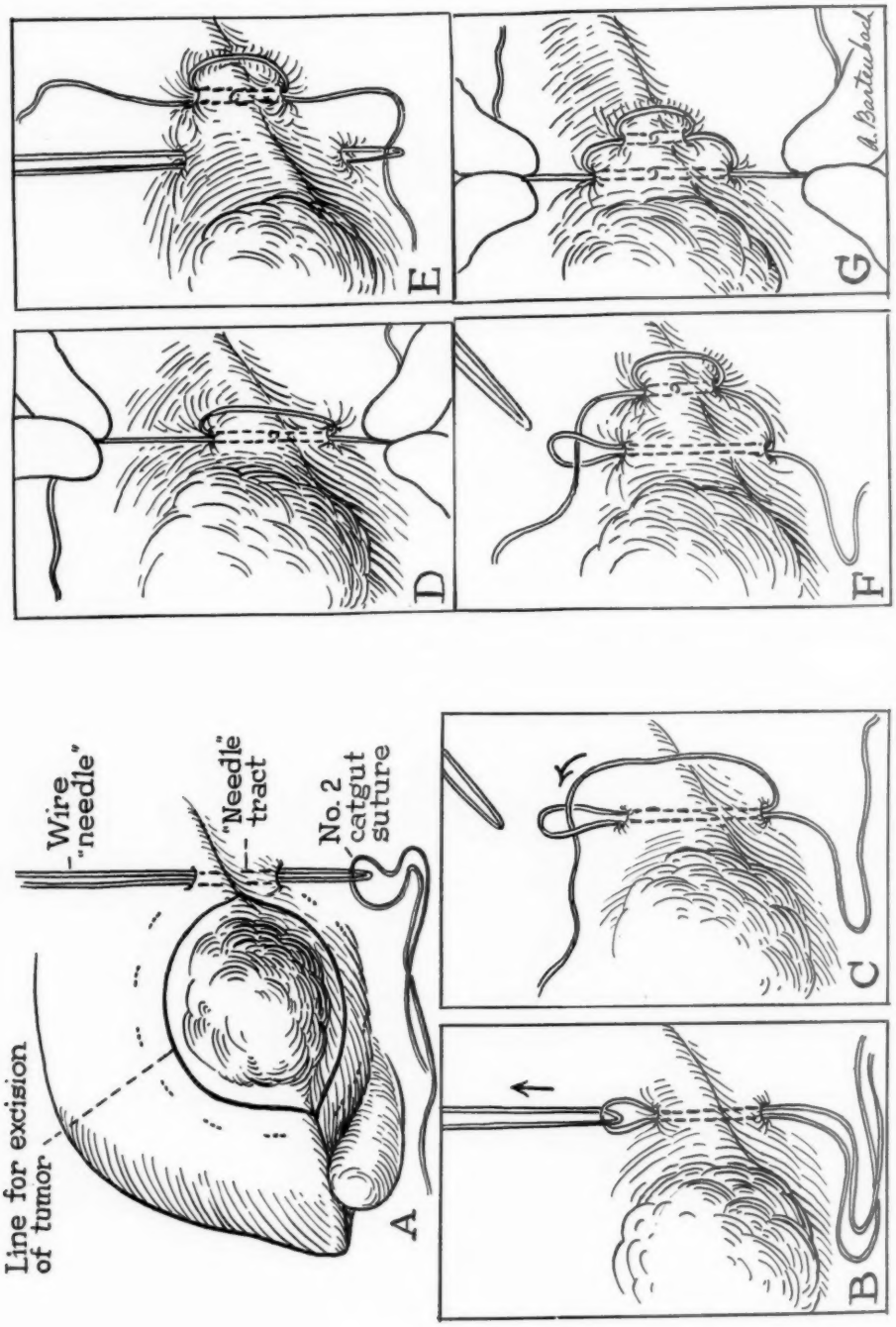


Fig. 1.—A to G, Illustrations of liver suture technique. Discussion in text.

One end of the suture is passed through this loop, the wire "needle" is removed from it, and the ends of the suture are drawn taut, allowing the interlocking junction of the suture to be pulled one-half the length of the needle tract (Fig. 1, *C*).

Tension is maintained upon the previously placed suture while these steps are repeated every 2 to 3 cm. until the portion of the liver to be resected has been completely encompassed.

Transection of the liver parenchyma outlined by the hemostatic suture is performed approximately 1 cm. adjacent to it (Fig. 1, *A*).

Hemostasis is completed by ligating the few small arteries which may continue to bleed from the cut surface.

## DISCUSSION

The liver suture technique described by Terrier and Auvray[5] is, with modifications, similar to the method outlined above. The interrupted mattress suture has been the most commonly employed hemostatic suture method of the many others which have been advocated for partial hepatectomy. With the mattress suture technique the average blood loss in large resections of the liver has been approximately 1,000 c.c.[1-4, 6] The "cobbler stitch" technique herein advocated (Fig. 1, *A* to *G*) is superior for the following reasons:

1. The long, blunt-pointed, flexible, bent wire passes easily through thick portions of liver parenchyma and does not puncture hepatic vessels or large bile ducts (Fig. 2, *A* and *B*).

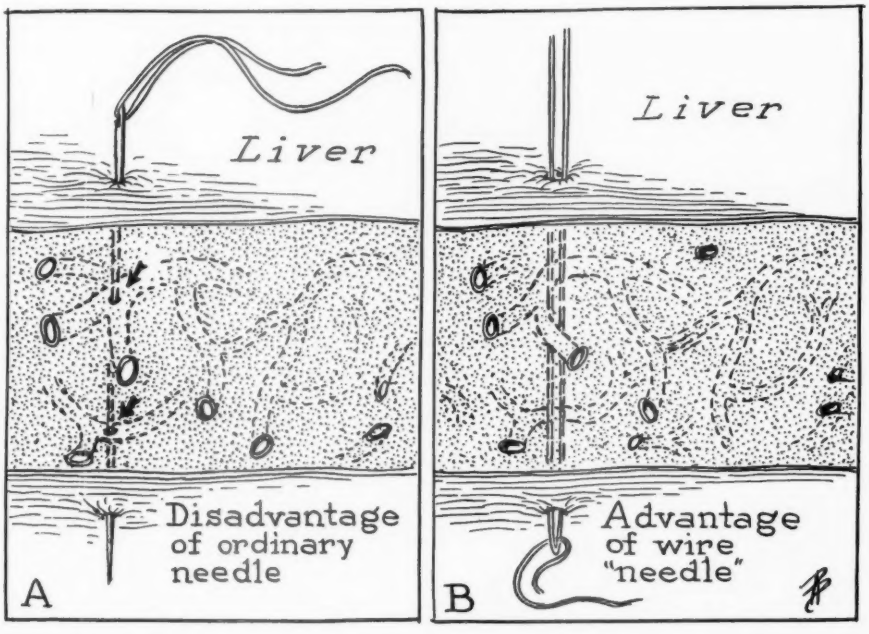


Fig. 2.—*A* and *B*, Illustrations of the advantages of flexible needle. Discussion in text.

2. There is less danger of tearing the liver upon tightening this suture because the shearing force is more equally distributed about the circumference of the encompassed parenchyma than when interrupted mattress sutures are drawn taut.

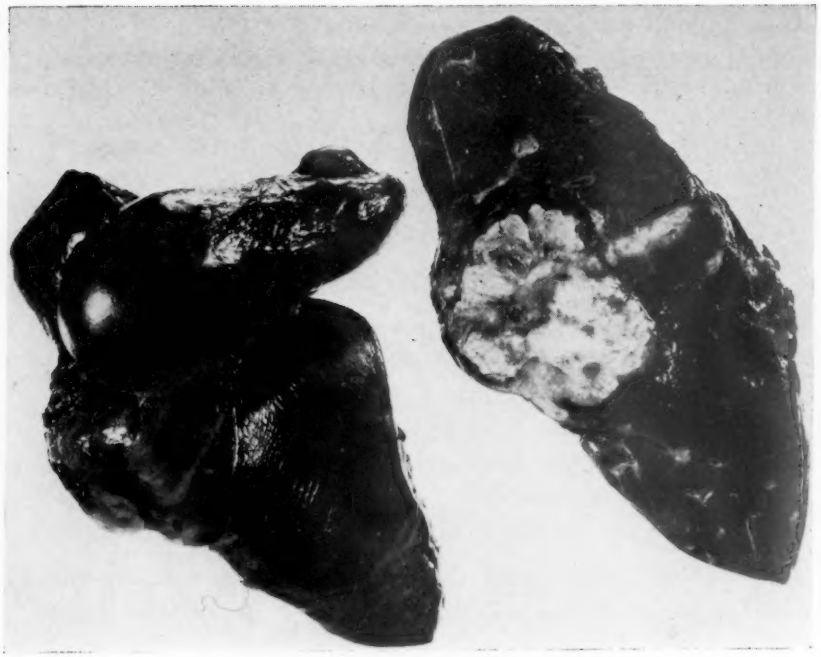

Fig. 3.

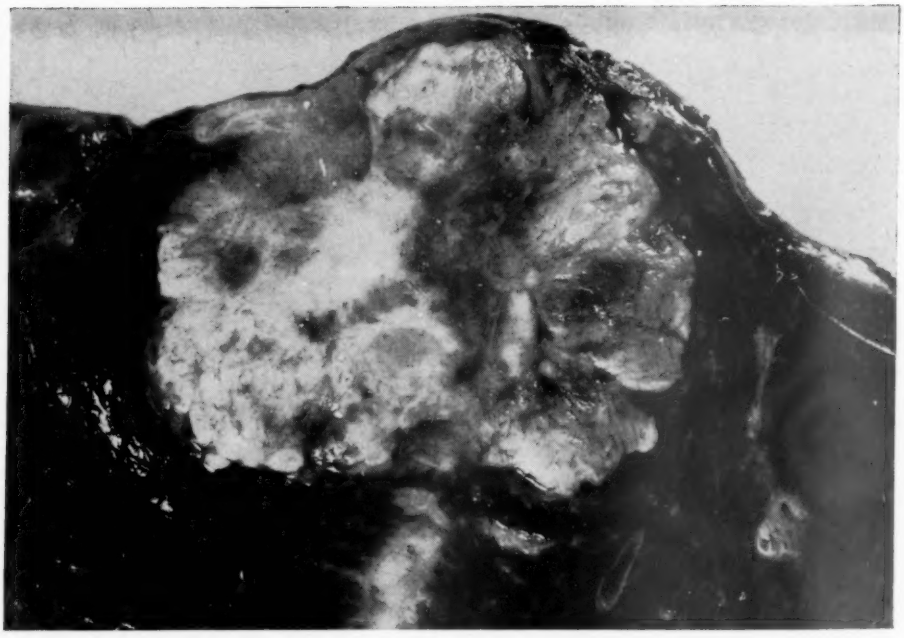

Fig. 4.

Figs. 3 and 4.—Photographs of gross specimen of tumor resected from Patient G. S.

3. The "cobbler stitch" is simple, rapidly placed, and does not allow any portion of the liver adjacent to the proposed line of resection to escape enclosure.

4. The suture encompassing a segment of the liver does not slip from this segment because it is continuous with that surrounding other adjacent segments. The "cobbler stitch" liver suture allows massive resections of liver with minimal blood loss (Table I) and lessened danger of air embolism. The major bile ducts to the remaining liver are not so likely to be injured by this technique because visualization of them is not hindered by bleeding. They are also easily avoided because the blunt wire needle can be accurately inserted through thick portions of liver.

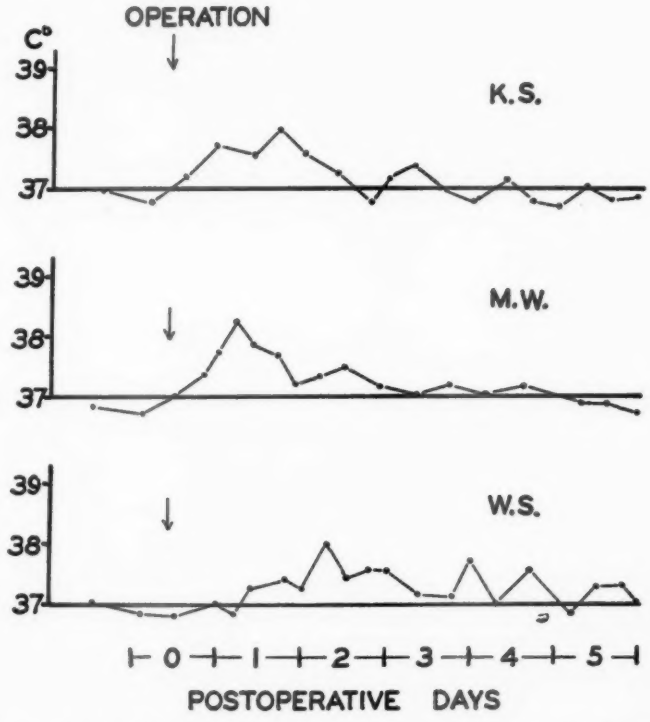


Fig. 5.—Temperature charts of three patients listed in Table I. All patients drained with sump catheter technique.

Many intrahepatic bile ducts are severed when large portions of liver are removed. Some bile leakage may thus occur. Drainage of the area by the sump catheter technique for seven to ten days helps to avoid the morbidity which may otherwise attend the intraperitoneal collection of bile (Fig. 5).

Large lacerations of liver parenchyma seen in military and civilian life can be handled rapidly with minimal blood loss by means of the "cobbler stitch." The suture should be placed so as to encompass the lacerated area. Resection of the traumatized portion of liver by this means accomplishes complete hemostasis and removes devitalized tissue. The use of packs, Gelfoam, and other hemostatic agents is unnecessary.

SUMMARY

A new hemostatic suture technique was used in the successful resection of three primary liver tumors. This method of suture is simple and widely applicable. The suitability of this method in traumatic liver damage is discussed.

REFERENCES

1. Brunschwig, A., and Smith, R. R.: Resection of Hemangioma of the Liver, Ann. Surg. **135**: 125, 1952.
2. Keen, W. W.: Report of a Case of Resection of Liver for Neoplasm. Table of 76 Cases of Resection of Liver for Hepatic Tumors, Ann. Surg. **30**: 267, 1899.
3. Longmire, W. P., Jr., and Scott, H. W.: Benign Adenoma of the Liver, SURGERY **24**: 983, 1948.
4. Rosenberg, D., and Ochsner, A.: Primary Carcinoma of the Liver, SURGERY **24**: 1036, 1948.
5. Terrier, F., and Auvray, M.: Les tumeurs du foie. Étude sur la résection du Foie, Rev. Chir. **18**: 706, 1898.
6. Warvi, W. N.: Primary Tumors of the Liver, Surg., Gynec. & Obst. **80**: 643, 1945.

# A NEW CLAMP AND CLAMP TECHNIQUE FOR FULL-THICKNESS MYOCARDIAL RESECTION

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GORDON MURRAY,[2] in 1947, suggested tentatively that in selected cases the best treatment of acute coronary occlusion in the human subject might be immediate surgery. This method, he argued, would not only offer a better chance of survival after severe infarction from major occlusion, but would also eliminate all the effects of the occlusion, including acute cardiac rupture, aneurysm formation, and subsequent rupture of the aneurysm. Murray tested the method in experimental animals but it does not seem to have been extended to human subjects.

Excisional surgery also seems rational in the management of dilatation of the ventricle, which, as Burch and his associates[1] have pointed out, performs its function of "human cardiac pump" under a definite mechanical handicap when it is dilated.

Finally, excisional surgery is a theoretical possibility in the treatment of localized tumors of the heart, though the fortunate combination of a tumor recognized early, sufficiently small for resection, and of a pathologic nature amenable to surgery is, of course, unlikely to be encountered very often.

To our knowledge, the only instance of excisional ventricular surgery to be described in the literature, in addition to Murray's experimental demonstration, is the resection of a ventricular aneurysm by Likoff and Bailey.[3] Myocardial aneurysm is a fairly frequent consequence of myocardial infarction and it remains asymptomatic, according to these observers, in less than half of all cases.

Although we are fully aware that the theoretical value of myocardial resection in a diseased and dilated heart might be overbalanced by the risks of the procedure, we have thought it worth while to develop in our laboratory a technique for the resection of full-thickness portions of the walls of both the right and the left ventricle. In addition, and as a matter of necessity, one of us (S. F. S.) has devised a clamp to be used for this purpose.

The excision of full thicknesses of the right ventricle, to which we first turned our attention, was accomplished with relative ease with the clamps devised by Potts, Glover and Satinsky and ordinarily used in vascular surgery. These clamps, however, proved inefficient when the same procedure was attempted on the left side. This was partly because of the increased thickness of the muscle on this side and also because of its greater friability, which increased

This investigation was supported by funds from the Tulane University Council on Research (Grant C-79-155) and from the Louisiana Heart Association (Grant C-445).

Received for publication Sept. 16, 1955.

Fig. 1.

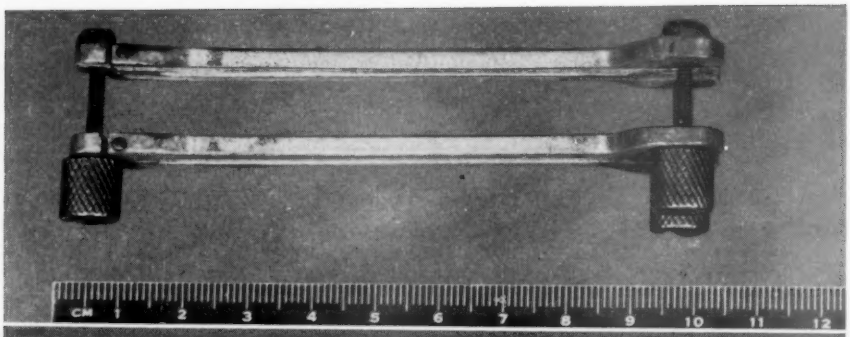


Fig. 2.

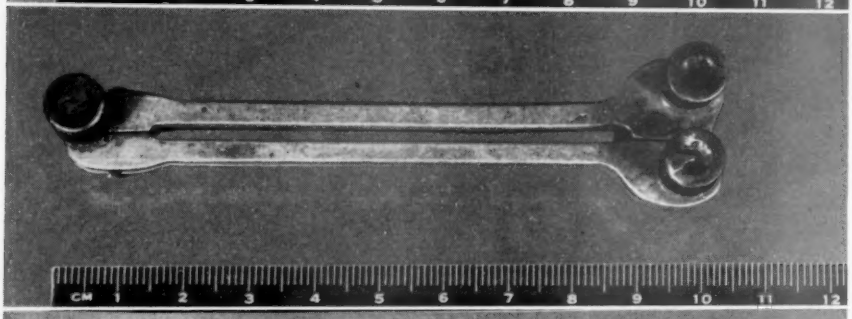


Fig. 3.

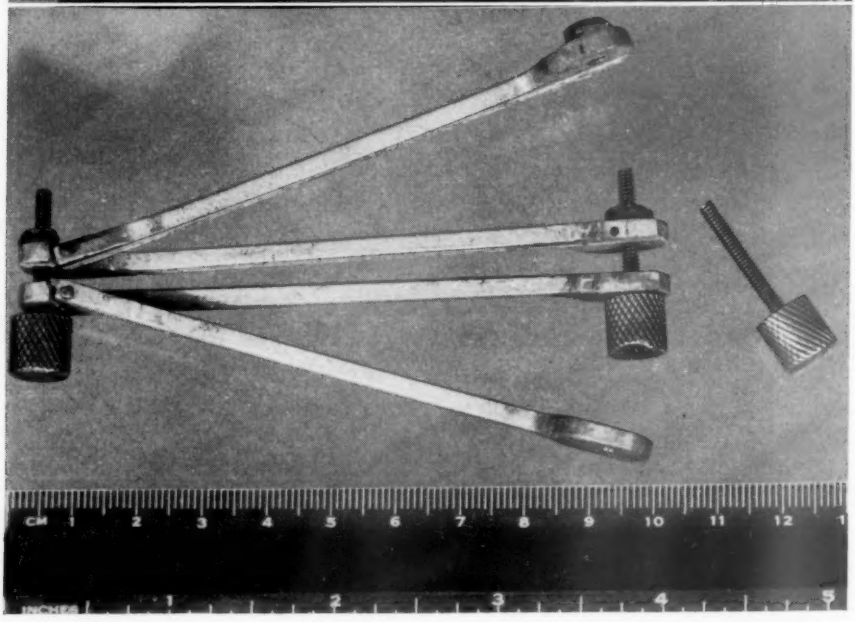


Fig. 1.—Clamp for myocardial resection, open, viewed from above.
Fig. 2.—Clamp for myocardial resection, closed, lateral view.
Fig. 3.—Clamp for myocardial resection with upper jaws swung open on pivot. Lower jaws are still approximated.

the risk of hemorrhage, even in the normal, healthy tissues of the animals on which we were working. Conceivably, these dangers would be much greater in a diseased, dilated, and pathologically thickened myocardium.

A clamp used for resection of the myocardium must meet several criteria:

1. It must be long enough to include the entire area to be resected. The clamps presently available are not long enough for this purpose, as Likoff and Bailey[3] learned in the resection of the ventricular aneurysm just mentioned; they were obliged to suture a portion of the sac without benefit of any clamp at all.

2. The clamp must not slip.

3. The amount of pressure exerted by the jaws must be susceptible to careful control. The pressure must be sufficient to prevent hemorrhage, but at the same time it must not be great enough to damage to any significant degree the portion of myocardium held in the jaws of the clamp which is left in situ when the grip is released.

## DESCRIPTION OF CLAMP

The clamp developed to meet these criteria (Figs. 1 to 3) consists of an upper and lower set of jaws each of which measures 10.5 by 0.4 by 0.4 cm. The instrument is thus small enough to manipulate within the chest wound and the pericardial incision, and there are no cumbersome handles to protrude from either incision.

The jaws are approximated at one end by a single knurl-headed screw. The upper set of jaws is pivoted at this end. At the other end, the upper and lower sets of jaws are approximated by separate knurl-headed screws. The upper jaws can therefore be manipulated separately (Fig. 3). After the myocardium is grasped between the upper and lower jaws, the screws can be adjusted to obtain the necessary amount of pressure. Between the upper and lower sets is a slot (Fig. 1) 0.2 cm. in width, through which a continuous suture is applied before the diseased myocardium is excised (Fig. 4).

The inner surfaces of the jaws are grooved, to prevent slipping. Although this has been no special problem in experimental animals, it might be that this hazard would be further eliminated if the surfaces were cross-hatched, on the principle employed in the Oschner diamond jaw needle holder. Still another possibility that has been suggested is the transverse insertion of two or three pins in the distal (upper) jaws.

## TECHNIQUE

The steps of the myocardial resection are as follows:

(1) The chest is opened in the fifth left interspace, by the standard technique. (2) The pericardium is incised and the pericardial flaps are held open by stay sutures. (3) Three traction sutures of braided no. 1 silk are inserted in the area of myocardium involved, care being taken to avoid major branches of the coronary artery and the papillary muscles in the cavity of the ventricle. (4) The myocardial wall is tented by traction on these sutures while the clamp is applied and the screws are tightened just enough to exclude this section of

the myocardium from the remainder of the ventricular cavity. The diseased portion protrudes above the upper set of jaws. (5) The myocardium is sutured through the slot in the clamp (Fig. 4) with a continuous mattress suture of

Fig. 4.

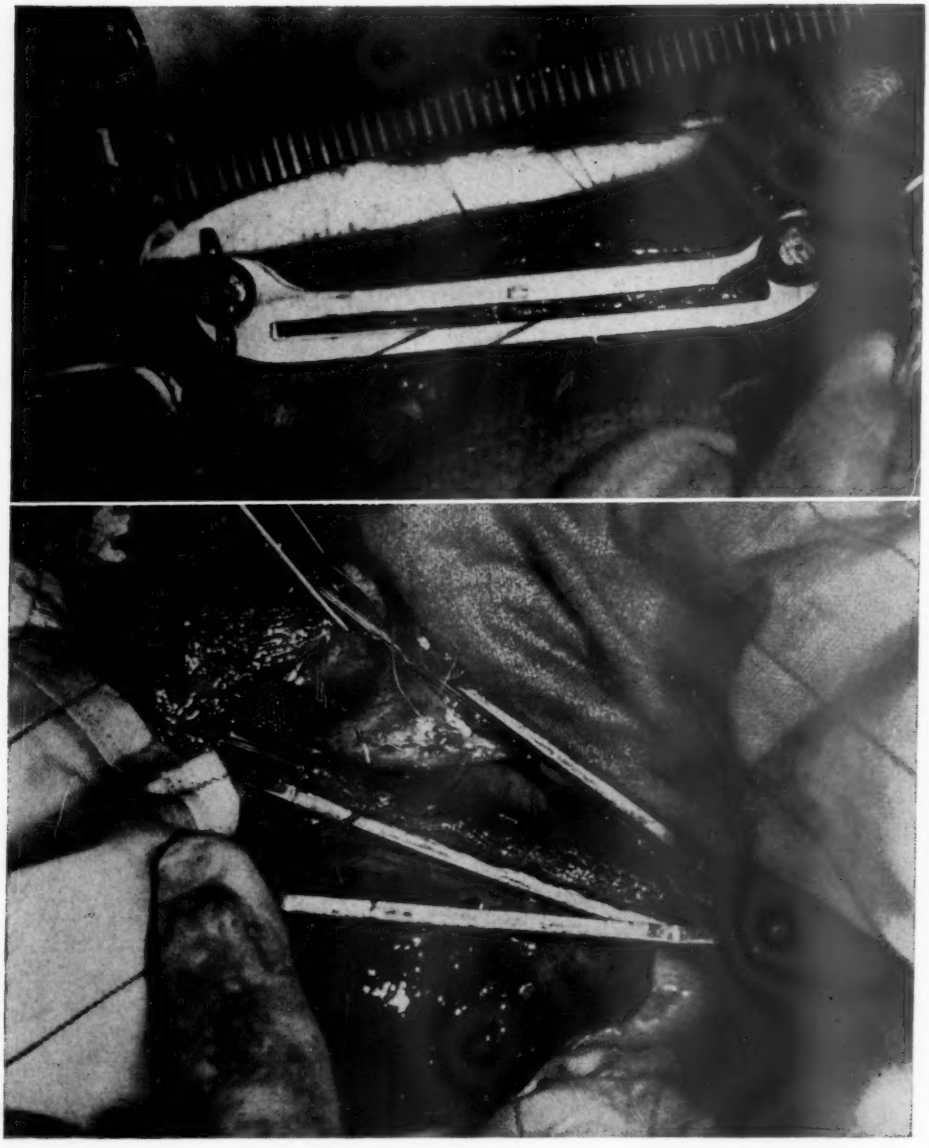

Fig. 5.

Fig. 4.—Application of first suture, through slot in closed clamp in myocardial resection.
Fig. 5.—Application of second suture in myocardial resection, with upper jaws of clamp open and swung out of the way.

No. 1 braided silk on an atraumatic thoracic needle. (6) The myocardium is resected level with the upper set of jaws. (7) The upper jaws of the clamp are swung open (Fig. 5) and a second continuous mattress suture is applied

to the cut end of the myocardium, after which the screw on the lower jaws is loosened and the clamp is removed. (8) The pericardial and thoracic incisions are closed by the usual technique.

## COMMENT

This clamp has been used to resect full thicknesses of the right ventricular wall in 5 dogs and of the left ventricular wall in another 7 dogs. Two deaths occurred, early in the series, after resections of the left ventricle. The first death occurred on the fifth postoperative day, presumably from cardiac failure. The second dog, after being apparently well for 3 weeks, died suddenly on the twenty-first day. Autopsy revealed the pericardium under tension from a serous effusion, and serosanguineous collections in the pleural and peritoneal cavities. The other dogs all recovered rapidly and were usually up and about within twenty-four hours after operation. They showed no signs of distress and no clinical evidence of cardiac failure in the periods before they were sacrificed.

Complete details of this technique will be published elsewhere, together with a description of the healing process in the pericardium, the electrocardiographic changes observed after operation, and the clinical course of the surviving dogs.

## SUMMARY

With the idea that resection of full-thickness portions of diseased myocardium may become a clinical reality, a special clamp has been devised for this purpose, together with a special technique for its use. The two deaths in the 12 experimental animals occurred early in the series. The clamp technique proved satisfactory in the other 8 animals, which showed no clinical deviation from normal in the periods of time which elapsed before they were sacrificed.

Appreciation is expressed to Dr. Julius Friedman and Dr. Robert Nieset, both of the Department of Biophysics of the Tulane University School of Medicine, for their cooperation and helpful suggestions in this investigation and for their assistance in the development of the clamp described.

## REFERENCES

1. Burch, G. E., Ray, C. T., and Cronvich, J. A.: Certain Mechanical Peculiarities of the Human Cardiac Pump in Normal and Diseased States, Circulation **5**: 504-513, 1952.
2. Murray, Gordon: The Pathophysiology of the Cause of Death from Coronary Thrombosis, Ann. Surg. **126**: 523-534, 1947.
3. Likoff, William, and Bailey, Charles P.: Ventriculoplasty: Excision of Myocardial Aneurysm. Report of a Successful Case, J. A. M. A. **158**: 915-920, 1955.

# Case Reports

## PERITONEAL CAVITY WITH TWO COMPARTMENTS

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THE following rare and unusual condition consisting of a peritoneal cavity divided by a double-layered membrane into an anterosuperior compartment which contained the abdominal viscera normally contained in the peritoneal cavity and a posteroinferior compartment which contained approximately 6 L. of fluid was diagnosed at operation and is hereby reported.

### CASE REPORT

*History.*—The patient was a 24-year-old, twice-married, white woman, admitted to the hospital on Nov. 27, 1954. She and her friends had noted a questionable enlargement of the abdomen the first half of the preceding year, and during the past six months the enlargement had become very definite. For six months preceding admission she had abdominal discomfort, gas pains, and constipation with two or three hard green stools a week. She had experienced dyspareunia since her second marriage in February, 1954, in contrast with a previous marriage during which she experienced no dyspareunia. Surgical scars on her abdomen had widened during the past year. Her menarche occurred at age 13 or 14, and her menstrual periods had always been irregular, the menstrual flow lasting as long as seventeen days on one occasion and the periods occurring at intervals of one, two, or three weeks. Since her menarche she had never passed a period of more than four weeks without menstruation. She had never been pregnant. She denied urinary symptoms or loss or gain of weight.

*Past History.*—Appendectomy at age 9 years resulted in complications which necessitated five subsequent operations for infection and fistulas between the ages of 9 and 12 years.

*Family History.*—This proved noncontributory.

*Physical Examination.*—Examination revealed height 63 inches, weight 129 pounds, temperature 98.6° F., pulse 88, respirations 18, blood pressure 130/90.

The patient was a well-developed, well-nourished young white woman who did not appear ill except for a protruberant abdomen which resembled near-term pregnancy. She appeared alert, intelligent, and cooperative. The abdomen was diffusely enlarged and distended, most markedly in the lower regions, and several surgical scars upon the lower abdomen had widened to become diamond-shaped. There was a definite fluid wave, a diastasis recti, and a questionable ventral hernia of the lower abdomen. The abdomen was nontender and nonrigid except from the distention. No abdominal masses or solid organs could be palpated. Peristalsis sounds were normal. Vaginal examination revealed the cervix and uterus markedly displaced to the right, and there was a vague impression of a large cystic

Received for publication Aug. 8, 1955.

mass in the left adnexa and bulging downward into the cul-de-sac, but the cyst could not be delineated nor could its definite presence be ascertained by several examiners. Rectal examination contributed nothing additional. No other abnormalities were noted.

*Laboratory.*—Serology negative, white blood cells 6,000 with 48 per cent neutrophils, 7 per cent band forms, 35 per cent lymphocytes, 7 per cent monocytes, 1 per cent eosinophils, and 2 per cent basophils; hemoglobin 13.5 Gm.; hematocrit 44 per cent; erythrocyte sedimentation rate 4 mm. per hour; urinalysis normal; blood urea nitrogen 13.5 mg. per cent; blood glucose 92 mg. per cent; serum protein 7.9 Gm. per cent with 4.4 Gm. per cent albumin and 3.5 Gm. per cent globulin; A:G ratio 1.3; total cholesterols 174 mg. per cent with 72 per cent esters; alkaline phosphatase 4.9 S.J.R. units; cephalin flocculation negative in twenty-four hours, 1+ in forty-eight hours; serum bilirubin 0.8 mg. per cent; van den Bergh 0.1 mg. per cent direct, 0.7 mg. per cent indirect; Bromsulphalein 5 per cent retention.

*Roentgenograms.*—Chest negative; intravenous pyelogram normal; barium enema showed sigmoid markedly deviated to the right.

*Preoperative Diagnosis.*—No definite preoperative diagnosis could be made but ovarian tumor was considered the most likely possibility and exploratory laparotomy was believed warranted.

*Operation and Operative Findings.*—Upon entering the abdominal cavity through a left paramedian incision, considerable difficulty was encountered in determining exactly when the peritoneal cavity was entered. The difficulty was presumed at the time to be caused by the numerous adhesions resulting from previous surgery and inflammation. Difficulty in identifying anatomic structures was so considerable that a compressed, attenuated loop of small bowel was inadvertently partly transsected. Adhesions were then freed from the small bowel and the injured segment was identified as ileum and repaired by end-to-end anastomosis. Posterior to the loops of intestine, a thin, bluish membrane stretching across the lower abdominal cavity could now be seen. This was first thought to be the wall of a large ovarian cyst, and an attempt was made to free its lateral margins. Some progress was being made toward attaining this objective when the membrane was inadvertently torn. The cystic cavity contained a measured volume of 5,250 c.c. of clear, slightly opalescent fluid plus a small undetermined volume which escaped onto laparotomy pads and drapes before it could be aspirated. Specimens of the fluid were collected for laboratory examination.

The opening in the membrane was then enlarged and the interior of the cavity was inspected. It was found to be lined by a thin serous membrane which covered the fundi of the bladder and uterus, enveloped the round ligaments, ovaries, and salpinges, and partly enveloped the sigmoid colon, which entered the cavity on the left, and to have all of the usual anatomic features and reflections of normal pelvic peritoneum. Investigation of the superior, anterior, and lateral margins of the cavity revealed that it extended upward to a roughly conical apex which ended near the anterior surface of the third lumbar vertebral body. The anterior boundary was a thin membranous sheet posterior to all the intestine, the loops of which could be visualized through the membrane. The lateral boundaries curved convexly outward and downward from the midline into the flanks and then inward to the point where the round ligament enters the inguinal canal. The posterior wall was a thin membrane covering the great vessels, prevertebral fascia, and other retroperitoneal structures in the manner of normal peritoneum. The reflection of the cystic peritoneal membrane from the round ligaments and other structures was almost identical bilaterally. The only opening in the membrane was that through which the sigmoid colon entered the cystic cavity on the left.

The fimbriated ends of the salpinges were clubbed and appeared to be closed. The left ovary was slightly papillomatous on the surface and there was hydrops of the left salpinx. The left ovary and salpinx were removed and sent to the laboratory for frozen-section examination, which showed no malignancy. The right ovary contained a hemorrhagic cyst which was resected and also found to be nonmalignant. For lack of a better term, the cystic peritoneal cavity was designated as the posteroinferior peritoneal compartment.

What we have called the anterosuperior peritoneal compartment was then explored and found to contain the liver, stomach, small and large bowel (except part of the sigmoid),

and no abnormalities except some peritoneal adhesions. Close inspection of the anterior parietal peritoneum revealed a reflected edge at the level of a line drawn between the two internal abdominal rings, the reflected peritoneum turning upward and backward over the anterior membrane of the posteroinferior peritoneal compartment and creating a double-layered diaphragm-like membrane between the two peritoneal compartments. Attempts to illustrate diagrammatically the anatomic and topographic features of the two peritoneal compartments can be seen in Figs. 1 and 2.

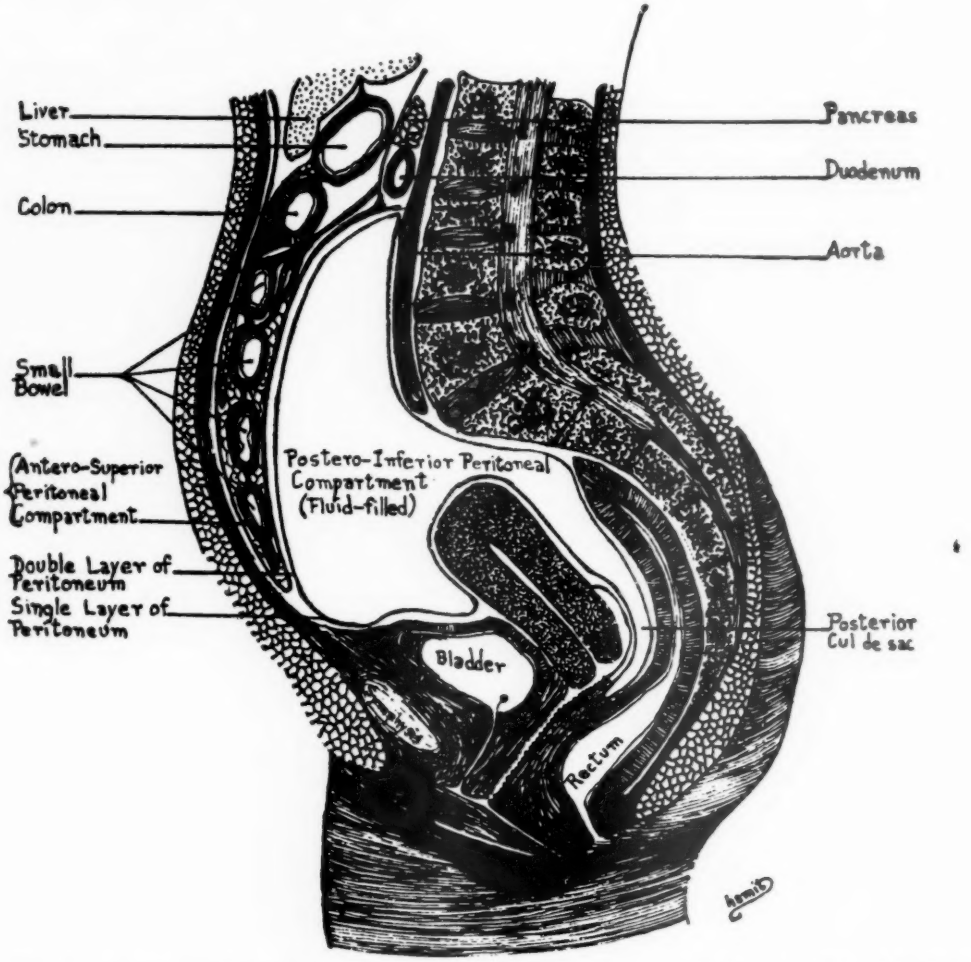


Fig. 1.—Anterosuperior peritoneal compartment shown to contain most of abdominal viscera and no fluid. Posteroinferior peritoneal compartment was reflected over the genitourinary organs of the pelvis and contained approximately 6 L. of fluid.

The diaphragm-like membrane between the two peritoneal compartments was excised and the incised edges of the parietal peritoneum were sutured together, thus forming a single peritoneal cavity and allowing the intestines to drop into the pelvis and obliterate the cavity formerly filled by fluid.

Laboratory studies of the fluid showed it to be relatively acellular, containing a few scattered lymphocytes, erythrocytes, and endothelial cells. Other pathologic diagnoses included hydrosalpinx of the left tube and ovary, hemorrhagic cyst of the right ovary, and chronic inflammation of the excised peritoneum. There was no evidence of specific inflammation or malignancy in any of the tissue removed.

*Postoperative Course and Follow-up.*—The patient made an uneventful recovery and when last heard from on May 31, 1955, had no evidence of reaccumulation of the fluid. Her only complaints were that her menstrual periods "still were not right but were improved" and that she tired easily. Otherwise she stated that she "felt like a new person."

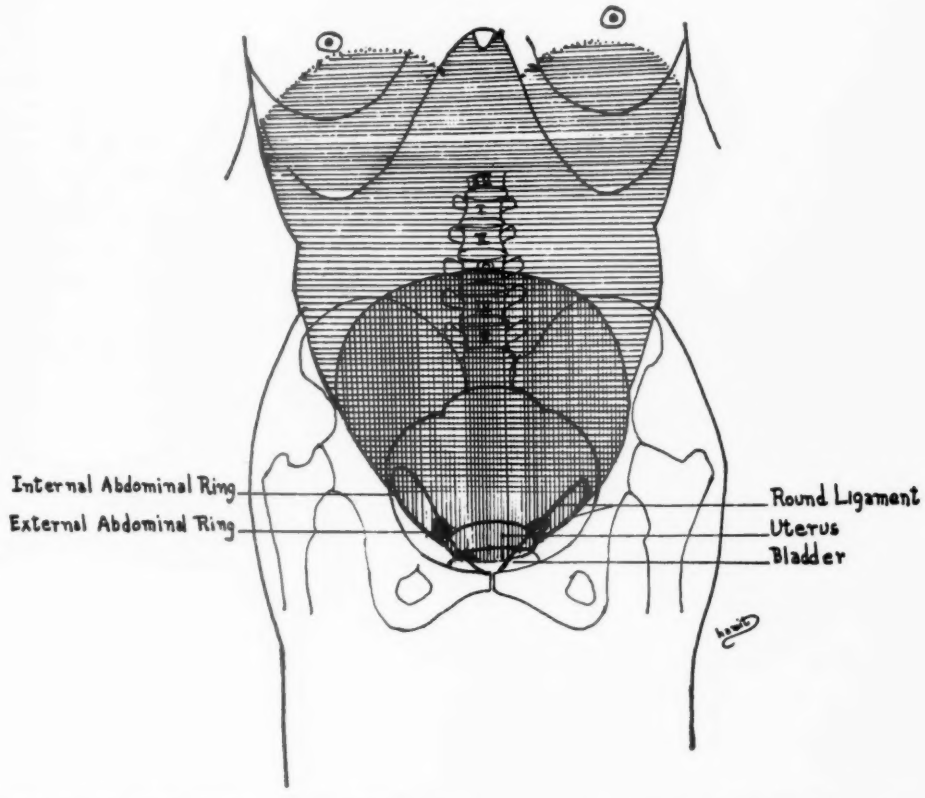


Fig. 2.—Diagrammatic representation of approximate topographic and anatomic extent of two peritoneal compartments. Vertical lines represent posteroinferior peritoneal compartment. Horizontal lines represent anterosuperior peritoneal compartment, the lowest horizontal line representing the peritoneal reflection of this compartment. Cross-hatched lines represent area where anterosuperior compartment overlapped the posteroinferior.

## REVIEW OF THE LITERATURE

A search of the literature reveals the previously described condition to be rare. The only similar cases found were those described separately by Warren[8] and Spencer.[6] Goldsmith[2] described a case which he called "invisceration" in which there was almost complete division of the peritoneal cavity into two compartments, the lower containing most of the abdominal viscera and neither containing any fluid, but Lipschutz, in commenting upon this case, stated that it was a right paraduodenal hernia. Trehair[7] reported a case of an abnormal peritoneal layer covering the small bowel; his case has the aspects of internal hernia. Gutierrez[3] did not describe a similar situation in his classic article on congenital peritoneal cysts, nor did Brites[1] in his article on peritoneal anomalies. Likewise, no description of this condition was found in the volumes upon the peritoneum by Hertzler[4] or in the monograph by Livingstone.[5] Hertzler expressed the opinion that the development of peritoneal cysts is the result of

an inflammation with fibrinous reaction and endothelial proliferation over the fibrinous mass to form a peritoneal leaflet. Warren stated that congenital peritoneal cysts may occur wherever there is a normal coalescence of two peritoneal surfaces and that the origin, etiology, and location of acquired cysts of the peritoneum are extremely variable. Like Hertzler, he attributed their origin to inflammatory reactions which may originate from mechanical, bacterial, or chemical irritants and stated that they commonly occur on or near the broad ligaments and in the cul de sac following salpingitis.

## CLINICAL FEATURES

Our patient and those of Spencer and Warren have some similar features. All were women, aged 24, 54, and 32 years, respectively. Warren's patient and ours had each had appendectomy several years previously, menstrual dysfunctions since the menarche, and both had married a few months previously. Spencer did not state whether or not his patient was married or had had an appendectomy but does indicate that she had a menstrual disturbance in that the condition developed shortly after the menopause. All had relatively normal clinical and laboratory findings except for signs and symptoms attributable to the cystic abdominal distention, and all responded to surgical treatment and remained well afterward. Both Warren's and Spencer's patients had evidence of varicosities. All the cases had a soft cystic lower abdominal mass which was difficult to outline and delineate. The fluid in Warren's patient was dark-amber and that of Spencer's patient was thin, brownish, and contained fibrin, and specimens of all three fluids showed unremarkable cellular content.

Warren treated his patient by marsupialization of the cyst to the skin, whereas Spencer did essentially the same thing by placing large drains from the cyst cavity to the skin. There is evidence that both of their patients suffered from episodes of peritonitis postoperatively before finally healing. It is suggested that the method used in the treatment of our patient is preferable to marsupialization or drainage to the exterior in that the danger of peritonitis is alleviated and the patient's postoperative hospitalization was short, uneventful, and she has remained well. It is recognized, at the same time, that excision of the intercompartmental membrane might not always be feasible or possible.

## COMMENTS AND DISCUSSION

Attempts to explain the etiology of the condition discussed herein seem to necessitate the use of large amounts of conjecture because of the rarity of the condition, if for no other reason. The possibility that our case represented a large cyst of Morgagni or a parovarian cyst was entertained briefly, only to be dismissed as unlikely because of the bilateral anatomic symmetry of the structure. However, this possibility is not entirely excluded. Another considered possibility was that the cystic cavity represented an old pelvic abscess cavity which had filled with fluid, perhaps incipient with the patient's difficulty with appendicitis. Here again this possibility was dismissed as rather fantastic because of the recent development of symptoms as compared with the time interval since the difficulty with appendicitis. Conversely, it was

also conjectured that the difficulty with the appendicitis may have been caused by the presence of a congenital peritoneal anomaly which the surgeon failed to recognize or understand.

The postulations of Warren and Hertzler that acquired peritoneal cysts originate in inflammatory processes merits considerable attention here in that there was evidence of chronic inflammation in the excised peritoneum and there was evidence of a bilateral chronic salpingitis in the clubbing and closure of both free ends of the salpinges. The contention that this was an acquired rather than a congenital lesion is also supported by its recent development, although delayed manifestations of congenital lesions are not unknown, for example, polycystic kidneys. The congenital origin of this structure is supported by the almost absolute bilaterally identical anatomic symmetry of the cystic compartment, but we are certainly at a loss to attempt to explain embryologically how it occurred. Again, if it is an inflammatory lesion, presumably caused by salpingitis or other pelvic inflammation, or if it is related to dysfunction of menstruation, why is it not seen more often since these proposed etiologic factors are so common and universal?

## SUMMARY

A rare and unusual case of a double-compartmented peritoneal cavity, one compartment being cystic and the other containing the abdominal viscera, along with a comparison and discussion of two similar case reports found in the literature is presented. Clinical features, possible origins, and the treatment of such conditions are also discussed.

## REFERENCES

1. Brites, G.: Quelques observations d'anomalies du péritoine et de la position de l'intestin chez l'homme, Folia anat. univ. conimb. **2:** 1-25, 1927.
2. Goldsmith, R.: Invisceration, Ann. Surg. **102:** 387-390, 1935.
3. Gutierrez, A.: Quistes de origen peritoneo-congenital; su Clasificación, Rev. cir. Buenos Aires **17:** 48-60, 1938.
4. Hertzler, A. E.: The Peritoneum, St. Louis, 1919, The C. V. Mosby Company.
5. Livingstone, E. M.: A Clinical Study of the Abdominal Cavity, and Peritoneum, New York, 1932, Paul B. Hoeber, Inc.
6. Spencer, W. G.: Large Intra-peritoneal (Paraovarian) Cyst Disappearing After Drainage, Brit. J. Surg. **10:** 424-425, 1923.
7. Trehair, E. B.: A Case Presenting an Abnormal Peritoneal Layer Covering the Small Bowel, J. Roy. Army Med. Corps **82:** 185-186, 1944.
8. Warren, K. W.: Peritoneal Cyst, Lahey Clin. Bull. **5:** 185-188, 1947.

# GASTROCOLIC FISTULA RESULTING FROM BENIGN GASTRIC ULCER

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IN THE autumn of 1954 we encountered our first case of spontaneous formation of a gastrocolic fistula resulting from a benign gastric ulcer. Because of its novelty in our experience the literature was reviewed in an effort to determine the frequency with which this complication of gastric ulcer occurs.

In 1925 Verbrugge[8] reviewed the literature up to that date and found only twenty-five cases of benign gastric ulcer perforating into the colon, and only one of these had occurred since 1903. A review of the literature since Verbrugge's report reveals four more cases. Wilkie[9] in 1934 reported a case of a 32-year-old man. Bailey and Knoll[1] in 1939 reported, among other cases, one of an Indian woman who developed a fistula between a simple gastric ulcer and the transverse colon. In 1948 Pein[7] reported an interesting case of a gastrocolic fistula in a 5-week-old infant resulting from a peptic ulcer of the greater curvature of the stomach. Briggs and Boswell[3] in 1952 added the fifth and last case found within the last fifty years.

## CASE REPORT

On Sept. 27, 1954, a 35-year-old married white woman was admitted to the Women's College Hospital for investigation of diarrhea. Her history began twenty years before when she had vomited gross blood for the first time. From that time onward she began to have upper abdominal pain an hour or more after eating, sometimes relieved by the taking of additional food. This persisted for several weeks at a time and recurred three or four times a year. At the age of 22 years she had had another small but definite episode of hematemesis.

The patient continued in this manner with recurrent bouts of indigestion until July, 1954. Since about July 25 she had had slightly more severe upper abdominal distress with the taking of food than usual. On August 4 she began to vomit such gross volumes of frank blood and blood clots that she had to be rushed into her neighborhood hospital. Over a period of four days she was given 4,000 c.c. of whole blood before the hematemesis stopped. On the same day on which she began to vomit blood, persistent severe diarrhea appeared, with up to 14 liquid movements per day. At first these movements were tarry, but after the hematemesis ceased they became merely partially liquid brown stools. They contained no obvious blood, pus, or mucus, but particles of recognizable undigested food were often seen. After ten days she signed herself out of this neighborhood hospital with the diarrhea still present.

The diarrhea and severe epigastric pain persisted over the next six weeks until her admission to the Women's College Hospital. She had to eat frequently in an effort to relieve the upper abdominal pain, which now radiated through to the back. Every small meal was followed by the passage of three or four semiliquid stools often containing undigested food. Despite the diarrhea, the patient had lost only ten pounds in weight.

Examination revealed an obese white woman weighing 207 pounds who was not acutely ill but was in obvious persistent distress. She rarely lay down because doing so

Received for publication Aug. 12, 1955.

increased the pain in the back, and she sat up most of every night drinking hot milk at least as often as every two hours. She had been taking the antispasmodics, mild sedatives, and gastric alkalis prescribed two months before without any appreciable improvement in the pain or diarrhea.

Physical examination aside from that of the abdomen was essentially negative. The abdomen was very obese. Tenderness was elicited over the entire epigastrium, but there were no palpable masses and no muscular resistance. The solitary abdominal scar was a lower right paramedian one which extended only three-quarters of an inch above the level of the umbilicus.

Fig. 1.

The red and white blood cell counts were normal, as was the blood smear. The hemoglobin content was 9.5 Gm. per cent. Examination of the stools revealed occult blood, but no pus and no specific bacterial or parasitic cause of the diarrhea. Radiologic examination by means of a barium enema showed the presence of a gastrocolic fistula (Fig. 1). A gastric series carried out subsequently failed to demonstrate the fistula. The barium did not pass from the stomach into the transverse colon, but only in the reverse direction. There was so much hurry of the gastric content into the upper small bowel that it was impossible, even under fluoroscopic examination, to demonstrate a peptic ulcer of either stomach or duodenum. It was not even possible to prove whether or not a gastroenterostomy existed.

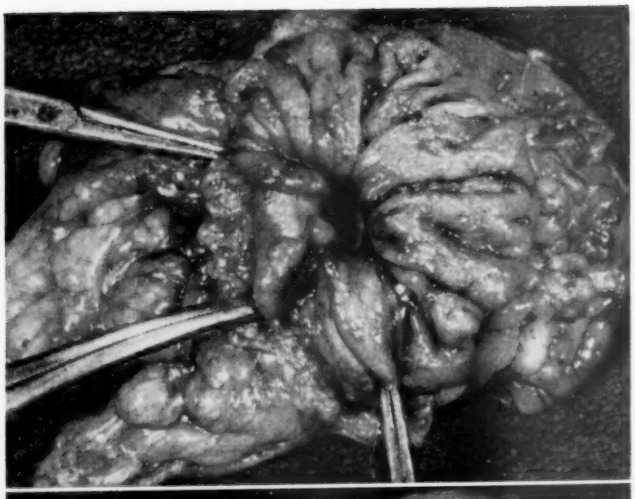

Fig. 2.

Fig. 3.

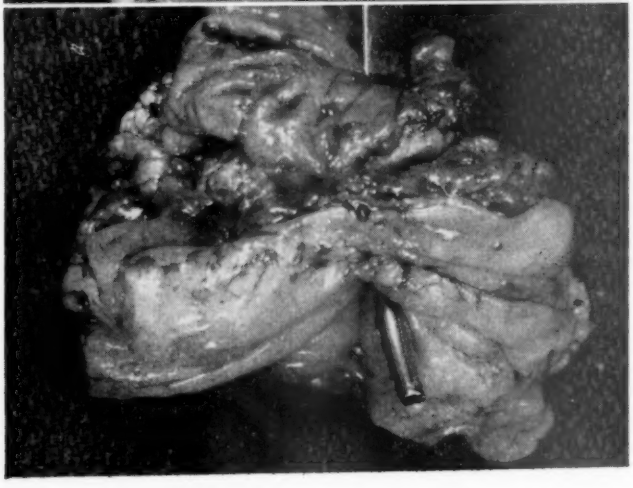

Fig. 4.

In our experience, gastrocolic fistula had almost invariably been associated with a gastroenterostomy previously performed for duodenal ulcer, and was due to a stomal ulcer which had perforated into the transverse colon producing the familiar gastrojejunocolic fistula. In this case, however, communication with the surgeon in another city who had removed the patient's appendix twenty years before, confirmed the patient's story and the mute evidence of the low situation of her abdominal scar, that no gastroenterostomy had been performed at the time of her only previous abdominal operation.

In the presence of a gastrocolic fistula of unrecognized etiology, it was felt that abdominal exploration would be rendered more safe by a preliminary defunctioning colostomy. On October 12 a colostomy of the hepatic flexure was made. Following this the patient's diarrhea ceased. The distal colon and rectum were thoroughly cleansed by irrigations. It was observed with interest that food taken by mouth did not escape into the distal colon to be passed by the rectum, but that whatever fluid was used as an enema for the rectum was invariably promptly vomited, and was easily recognizable as soapsuds, peppermint water, and so on. In other words, the gastrocolic fistula remained a one-way communication, colon content escaping readily into the stomach, but gastric content failing to escape into the colon.

At laparotomy on November 2 a benign peptic ulcer of the greater curvature of the stomach with a deep punched-out crater approximately 1 cm. in diameter was found. The base of the ulcer was firmly adherent to the mesenteric border of the transverse colon, and an inflammatory mass about the size of a walnut surrounded the fistula extending from the bottom of the gastric ulcer into the lumen of the colon. The fistula itself was several millimeters in diameter as is shown in Figs. 2 to 4.

A segment of the colon, including the fistulous opening, was resected, and an end-to-end anastomosis of the bowel was performed. A subtotal gastrectomy was then carried out, using the Billroth I type of reconstruction. The defunctioning colostomy was closed on November 26.

Undoubtedly, spontaneous communications between stomach and colon occur more frequently as a result of benign gastric ulcer than a review of the literature would indicate, because many cases are not reported. Nevertheless it is probably a rather rare complication because most benign gastric ulcers are situated along the lesser curvature of the stomach, and are thus not in close proximity to the transverse colon.

## REFERENCES

1. Bailey, W., and Knoll, W. V.: Gastrocolic Fistula, Radiology **32**: 347-350, 1939.
2. Bec, F.: De la fistula gastrocolique, Lyons, 1897, A. Rey.
3. Briggs, J. D., and Boswell, W. W.: Gastroduodenocolic Fistula Due to a Benign Gastric Ulcer: Case Report, Ann. West. Med. & Surg. **6**: 564-566, 1952.
4. Chavannaz, G.: Fistules gastrocoliques, Rev. Gynec. et chir. abd. **40**: 257, 1917.
5. Elsner, H.: Eine Dauerheilung einer Fistula gastrocolica, München. med. Wchnschr. **1**: 1386, 1903.
6. Firth, D.: A Case of Gastrocolic Fistula, Lancet **1**: 1061, 1920.
7. Pein, N. K.: Neonatal Gastrocolic Fistula, Lancet **2**: 53-54, 1948.
8. Verbrugge, J.: Gastrojejunocolic Fistulas, Arch. Surg. **11**: 790-808, 1925.
9. Wilkie, D. P. D.: Jejunal Ulcer, Ann. Surg. **99**: 401-409, 1934.

# PANCREATITIS OCCURRING IN HETEROTOPIC PANCREATIC TISSUE

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OBSTRUCTION to the normal flow of pancreatic secretions has been widely accepted as an important etiologic factor in the development of acute pancreatitis. Rich and Duff,[8] as well as others, have attributed the development of edematous pancreatitis to the distension and rupture of pancreatic acini and ductules behind the obstruction with a resultant escape of pancreatic juice into the interstitial tissue. They suggested that under certain conditions the extravasated pancreatic juice may cause necrosis of the walls of neighboring arteries and veins, transforming edematous pancreatitis into hemorrhagic pancreatitis. In 13 of the 24 cases of pancreatitis which they studied, epithelial metaplasia of the smaller pancreatic ducts and acinous dilatation were found. Although obstruction to the flow of pancreatic secretions may occur at different points in the ductal system and may be caused by different factors, they concluded that in most cases of pancreatitis the main pancreatic duct is unobstructed while the branches of the duct within the pancreas are blocked.

Other authors[1, 3, 7] consider that obstruction at the papilla of Vater with a reflux of bile through a common channel into the pancreatic duct is the usual pathogenetic mechanism of acute pancreatitis, and that it is probably caused by a stone or by a spasm of the sphincter of Oddi.

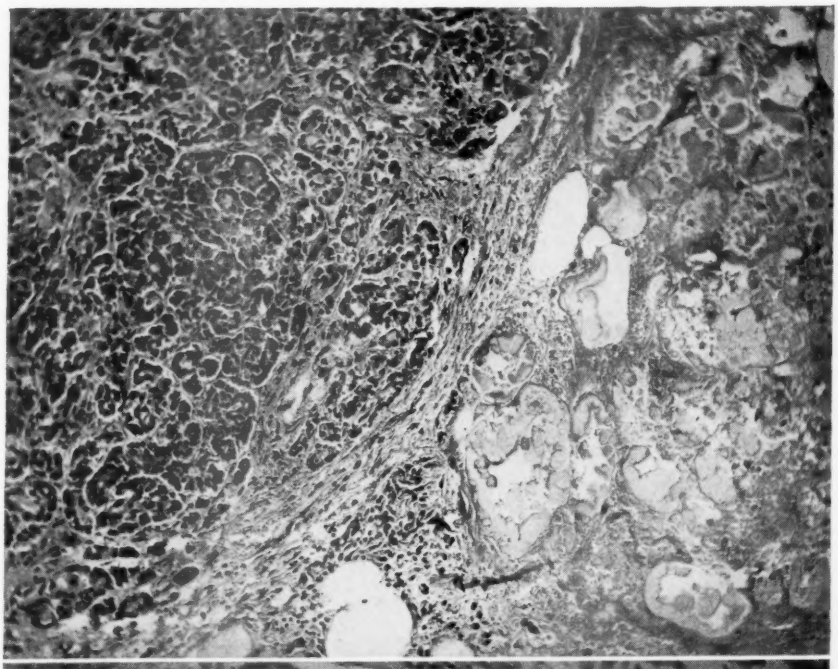
It is difficult to demonstrate regularly the presence of either of these conditions in patients who have pancreatitis. Based upon this theory of papillary obstruction, however, division of the sphincter of Oddi has been advocated[4] for the treatment of chronic or recurrent pancreatitis. More recently Bowers[2] has advocated transplanting the proximal end of the common duct into the jejunum to prevent reflux of bile into the pancreatic system of ducts.

Only one report has been found of a case of acute pancreatitis in which the acute process was confined to heterotopic pancreatic tissue while the pancreas was normal.[6] Reflux of bile, of course, could not be responsible for the pancreatitis in such heterotopic tissue.

The present report presents two cases of pancreatitis occurring simultaneously in the pancreas and in aberrant pancreatic tissue which was associated with the small intestine. Case 2 represents the first attempt to treat relapsing pancreatitis by retrograde drainage of the pancreatic duct into the jejunum. Despite continued patency of the anastomosis the course of the disease was not altered.

Received for publication Aug. 15, 1955.

Fig. 1.



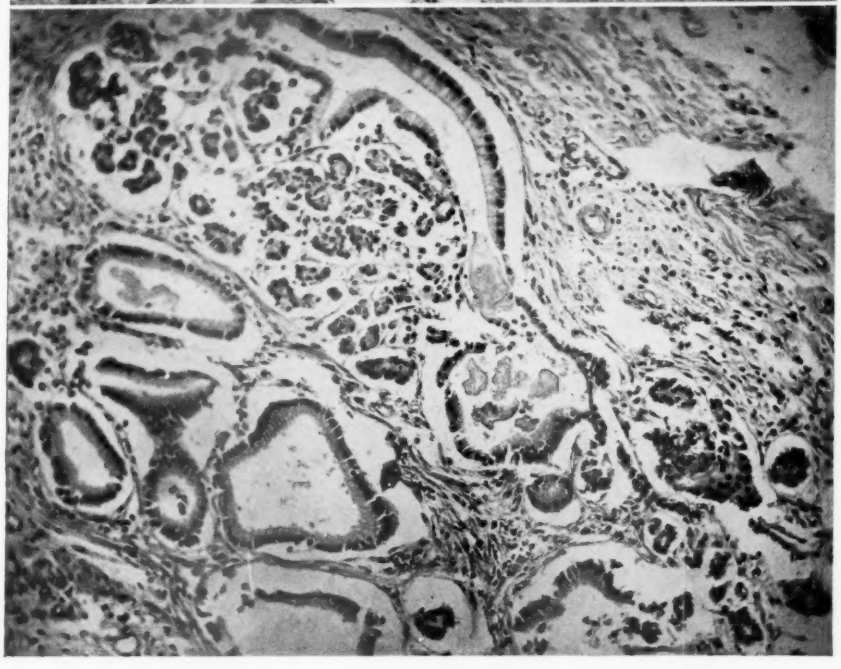


Fig. 2.

Fig. 1.—Case 1. Section from pancreas showing edema and necrosis of surrounding tissue and pancreatitis.

Fig. 2.—Case 1. Section from heterotopic pancreatic tissue of the Meckel's diverticulum showing dilatation of pancreatic ducts and destruction of acini.

## CASE REPORTS

CASE 1.—A 47-year-old white man was admitted to hospital July 7, 1948, after he had fallen unconscious on the street.

He had not felt well for about three years and had been unable to work for six months. His condition was characterized by frequent spells of nausea and vomiting, poor appetite, and yellowing skin. For the past month he had complained of a severe low-back pain. Over a period of seventeen years the patient had consumed large quantities of alcoholic beverages.

The patient was a well-developed, deeply jaundiced, critically ill white man. His skin and mucous membranes showed marked dehydration. Blood pressure was 128/76 and pulse was 104. Heart sounds were of poor quality. The abdomen was moderately distended and tympanitic with fullness in the flanks. No shifting dullness was demonstrated. The liver was palpable six fingerbreadths below the costal margin. Marked muscle spasm prevented palpation of other organs. Rectal examination was negative. Dark brown guaiac positive stool was present in the rectum. Neurological examination was normal.

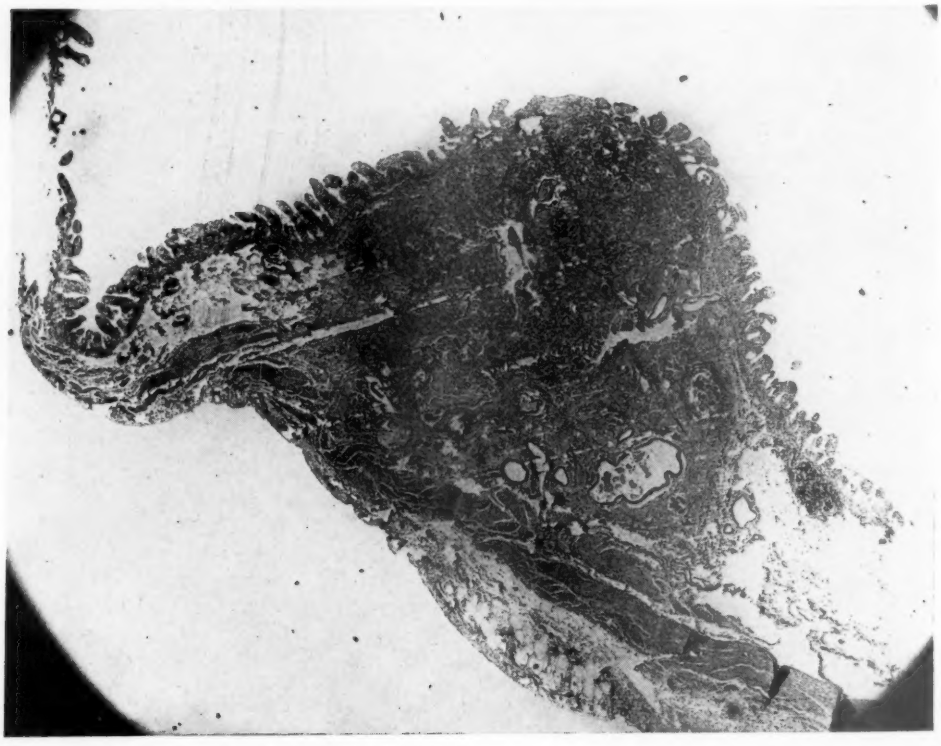


Fig. 3.—Case 1. Low magnification of heterotopic pancreatic tissue in Meckel's diverticulum.

Laboratory examination showed that urinalysis was negative; prothrombin time, 30 seconds, or 50 per cent of normal; red blood cell count, 3.8 million; and white blood cell count, 7,000.

The patient's condition rapidly deteriorated and he died on July 9, 1948.

*Autopsy.*—The skin was deeply jaundiced. The liver, which was morbidly enlarged (3,400 grams) showed no gross evidence of the scarring or fibrosis of a cirrhotic process. Just inferior to the transverse colon was a necrotic hemorrhagic process that involved the greater omentum, the mesocolon, and the root of the mesentery to the small intestine. This process seemed to originate in the region of the pancreas. The pancreas was large and firm on the surface but, on cut section, showed many areas of fat necrosis and hemorrhage. These

areas were found throughout the head, body, and tail of the gland, more marked in the head but still plentiful in the body and tail. Probing the pancreatic ducts did not reveal any calculi and no cysts were seen.

About 40 cm. from the ileocecal valve, a typical Meckel's diverticulum measuring 3 by 2 by 2 cm. was found, in the tip of which was a firm nodule, 1 cm. in diameter.

*Histopathology.*—The hepatic cells showed severe fatty degeneration although there was no evidence of a hepatitis. Sections of the pancreas verified the acute pancreatitis and fat necrosis. The nodule in the tip of the Meckel's diverticulum was composed of pancreatic tissue with acini and ducts containing calculi. An inflammaory process was present in this segment of pancreatic tissue that was similar to the process seen in the pancreatic gland (Figs. 1 to 3).

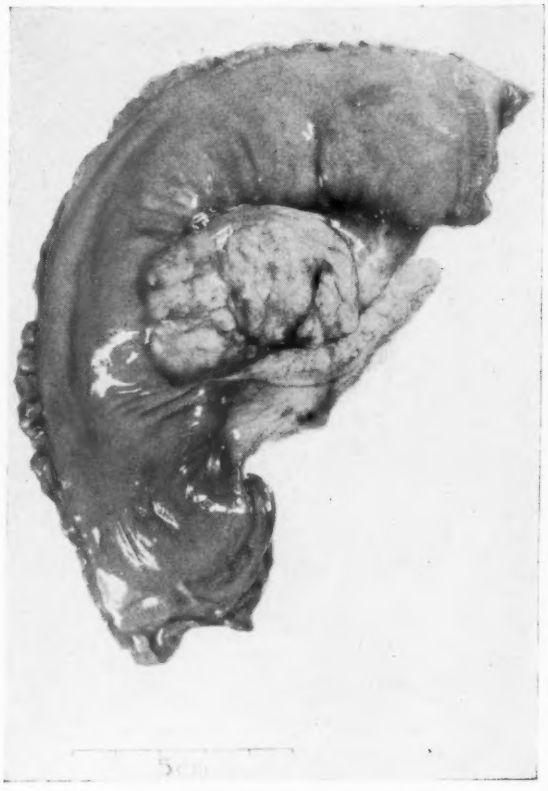


Fig. 4.—Case 2. Resected segment of jejunum with attached heterotopic pancreatic tissue.

CASE 2.—A 33-year-old man was admitted to the hospital Jan. 22, 1951, complaining of abdominal pain of four days' duration, and diarrhea for twenty-four hours.

His first admission to hospital was in December, 1950, because of an attack of severe abdominal pain, nausea, and vomiting. At that time he was acutely ill; the abdomen was tender in the epigastrium and right upper quadrant with referred and rebound tenderness. Serum amylase was 598 units, urinary diastase 13,260 units, and serum calcium 10.5 mg. per cent. A diagnosis of acute pancreatitis was made and he was treated by nasal gastric suction and sedation. Response to therapy was satisfactory. Subsequent cholecystograms and a gastrointestinal x-ray series were normal.

Severe epigastric pain, nausea, and vomiting returned four days before the second admission and had persisted intermittently. During the ensuing three weeks after hospitalization he continued to have mild intermittent epigastric pain associated with nausea. The diagnosis at the time of operation on Feb. 16, 1951, was recurrent acute pancreatitis.

*Operation.*—The pancreas was thickened and firmer than normal. There was slight edema in the retroperitoneal tissues and several small patches of fat necrosis were visible. On the mesenteric border of the jejunum about 8 inches distal to the ligament of Treitz there was a large segment of heterotopic pancreatic tissue which measured 3 by 3 by 7 cm. (Fig. 4). There was gross evidence of a subacute pancreatitis involving this aberrant tissue that was similar in appearance to that about the pancreas itself. Although the pancreatic tissue was firm, there was a slight edema of the surrounding mesentery, and small areas of local fat necrosis were visible. The segments of jejunum and heterotopic pancreas were excised. It had been our original plan to perform a retrograde drainage of the pancreatic duct by resecting the tail of the pancreas and anastomosing the proximal

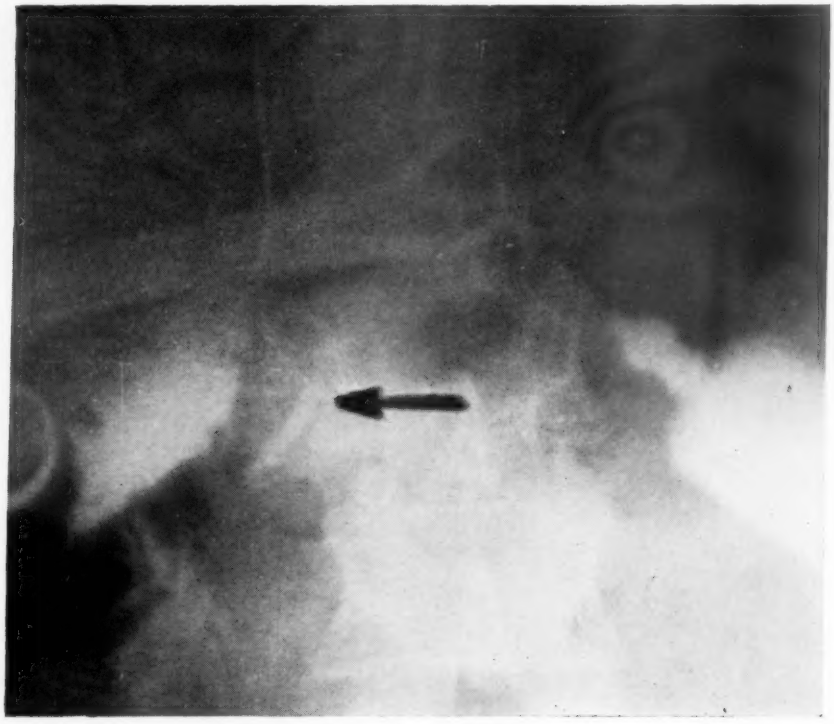


Fig. 5.—Case 2. Roentgenogram demonstrating injection of radiopaque solution through patent pancreaticodochojejunostomy 4½ months after anastomosis was established.

cut surface to a Roux Y jejunal limb. This procedure was carried out despite the evidence from the aberrant pancreatic tissue that the pancreatitis was probably not a result of obstruction in the main pancreatic duct. The operation failed to benefit the patient, who continued to have recurrent episodes of pancreatitis. Four and one-half months later, during abdominal operation, the caudal pancreaticodochojejunostomy was found to be patent (Fig. 5).

*Histopathology.*—Both the resected tail of the pancreas and the aberrant pancreatic tissue showed focal fat necrosis, prominent interstitial fibrosis, and subsiding chronic inflammation (Figs. 6 and 7).

## DISCUSSION

In contrast to the views expressed by Rich and Duff[8] that pancreatitis might be caused by epithelial metaplasia and obstruction of the smaller pancreatic ducts, reports in the surgical literature in recent years have emphasized the role of abnormalities of the major pancreatic ducts in the etiology of this disease.

Fig. 6.

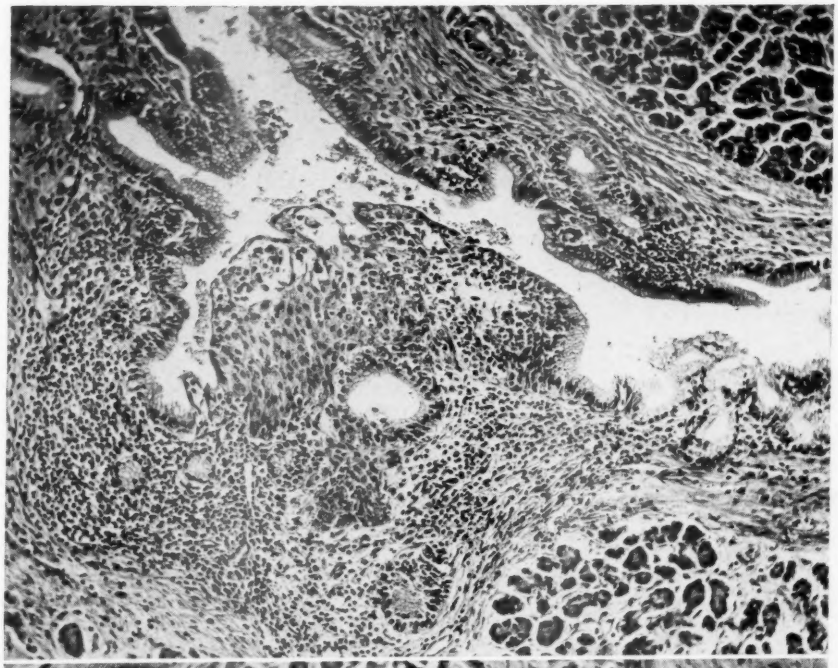


Fig. 7.

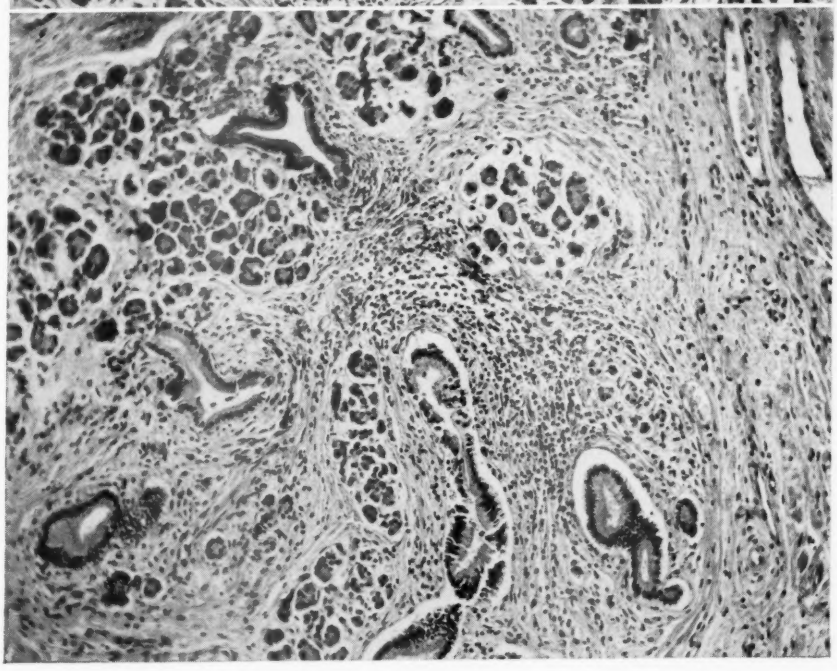


Fig. 6.—Case 2. Section of pancreas with chronic pancreatitis.

Fig. 7.—Case 2. Section of heterotopic pancreatic tissue also demonstrating chronic pancreatitis. Note similarity to process in pancreas proper.

Obstruction of the duct of Wirsung, or the reflux of bile into the pancreatic ducts, or both have been considered to be important etiologic factors in the production of relapsing or chronic pancreatitis.

In the two cases reported here, and in the case reported by Hasche-Klünder,[6] biliary reflux could not have been concerned with the production of the pancreatitis in the heterotopic tissues. It seems unlikely that other abnormalities of the major pancreatic ducts could have been responsible for this condition. The findings in these cases would indicate that the etiologic factors were of a more diffuse nature, such as those suggested by Rich and Duff. Areas of epithelial metaplasia in the smaller pancreatic ducts were present in both cases reported.

Failure of caudal pancreaticodochojejunostomy to afford relief in Case 2 also supports the view that interference with drainage from the duct of Wirsung was not an important etiologic factor. The caudal pancreaticodochojejunostomy performed on Feb. 16, 1951, is the first operation of this type that we have found in the literature. Duval[5] has reported symptomatic improvement following this anastomosis.

SUMMARY

Two cases of pancreatitis involving heterotopic pancreatic tissue as well as the pancreas are reported. Abnormalities of the major pancreatic ducts could not, of course, have been responsible for the pancreatitis in the heterotopic tissue. The first caudal pancreaticodochojejunostomy performed is reported. The operation failed to alter the course of the disease in this patient.

REFERENCES

1. Archibald, E.: The Experimental Production of Pancreatitis in Animals as the Result of the Resistance of the Common Duct Sphincter, Surg. Gynec. & Obst. **28**: 529, **1919.**
2. Bowers, R. F.: Choledochojejunostomy: Its Ability to Control Chronic Recurring Pancreatitis, Presented at the American Surgical Association Meeting in Philadelphia, April 29, 1955.
3. Cameron, A. L., and Noble, J. F.: Reflux of Bile up the Duct of Wirsung Caused by an Impacted Biliary Calculus, J. A. M. A. **82:** 1410, 1924.
4. Doubilet, H., and Mulholland, J. H.: Recurrent Acute Pancreatitis: Observations on Etiology and Surgical Treatment, Ann. Surg. **128:** 609, 1948.
5. Duval, M. K., Jr.: Caudal Pancreaticojejunostomy for Chronic Relapsing Pancreatitis, Ann. Surg. **140:** 775, 1954.
6. Hasche-Klünder, R.: Fettgeuebsnekrose im Nebenpankreas eines Meckelschen Divertikels, Chirurg. **20:** 82, 1949.
7. Opie, E. L.: The Relation of Cholelithiasis to Disease of the Pancreas and to Fat Necrosis, Am. J. M. Sc. **121:** 27, 1901.
8. Rich, A. R., and Duff, G. L.: Experimental and Pathological Studies on the Pathogenesis of Acute Hemorrhagic Pancreatitis, Bull. Johns Hopkins Hosp. **58:** 212, 1936.

# OSTEOGENIC SARCOMA

## Case Report of a Long-Term Survival

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IN DISCUSSING indications for hemipelvectomy,* Coley,[2] in 1951, listed osteogenic sarcoma as an absolute contraindication for the performance of this procedure. Under the circumstances it was felt that a publication of a long-term survival of a patient with osteogenic sarcoma treated by hemipelvectomy would be of some interest.

The first hemipelvectomy was performed by Bilroth[1] in 1891, but the first surgically successful case was reported by Girard[3] in 1895. The early surgical mortality of 70 per cent associated with this procedure has, in recent years, been reduced to 15 per cent.[6] Taylor and Rodgers[7] recently reported eighteen consecutive operations without a mortality.

The technical procedure utilized was the same standard operation so ably described in the reports by Pack and Ehrlich[5] and Gordon-Taylor.[4]

### CASE REPORT

L. L., a 37-year-old man, entered the Cedars of Lebanon Hospital on Feb. 18, 1948 with a history of pain in the left foot of 18 months' duration, increasing numbness and weakness of the left thigh and entire extremity of 5 months' duration, and progressive disabling pains in the left hip with inability to bear weight on the part of three weeks' duration.

The examination revealed a chronically ill, bed-ridden patient suffering marked pain in the left hip especially with changes in position and inability to normally use or bear weight on the left lower extremity. There was a 10 by 5 cm. palpable firm mass attached to the left iliac crest which extended into the pelvis as palpated through the left lower quadrant of the abdomen. A continuation of the mass was palpable as a 13 cm. bulge into the left buttock. There was marked atrophy of the left thigh and calf, numbness along the outer anterior surface of the thigh, and diminished knee and ankle reflexes. Rectal examination confirmed the presence of the large, hard mass fixed to the left side of the bony pelvis.

A complete bone survey was negative except for the tumor of the left iliac bone (Fig. 1). The intravenous pyelogram revealed a marked deviation of the left ureter to the right and a compression deformity of the left half of the urinary bladder (Fig. 2). The chest plate was negative.

The blood count revealed an R.B.C. of 4.5 million, Hg of 13.4 Gm., and C.I. of 0.87. The W.B.C. was 9,100 with a normal differential except for the 48 per cent lymphocyte count. The hematocrit was 41 per cent. The sedimentation rate was 32 mm. per hour, corrected Wintrobe method. Acid phosphatase was 7.5 units Shinowara modification King Armstrong method, normal less than 5. The alkaline phosphatase was 21.5 units King Armstrong, normal less than 12.

Received for publication Aug. 22, 1955.

*Interpelvi-abdominal operation, Interinnomino abdominal operation, Hindquarter amputation.

Preadmission needle biopsy of the mass was inconclusive. An open biopsy on February 20 yielded only reactive fibrosis and probably represented a piece of the capsule of the iliac tumor. A second open biopsy on March 9 was reported as osteogenic sarcoma of the left iliac bone.

Hemipelvectomy was performed by one of us (S. L. P.) on March 19 using the standard technique as described by Pack and Ehrlich[5] with one major exception. Due to the presence of the tumor overlying the anterior surface of the left sacroiliac synchondrosis, this joint had to be severed from the posterior aspect. In turning the patient onto his right side he went into shock, but this was counteracted successfully with the rapid administration of blood and the prompt execution of the surgical procedure.

Fig. 1.—Tumor involving almost the entire left iliac bone.

The pathologic report was as follows: The specimen consisted of the entire left leg with attached ilium, pubis, and ischium. The upper skin margin was at the inguinal ligament, the symphysis pubis, the perineum, above the trochanter and across the buttock.

A large mass filled the pelvis from the superior ramus of the pubis to the iliac fossa, projected laterally past the anterior superior spine and extended medially to the disarticulated sacroiliac joint. Its greatest diameter was about 21 cm. It projected posteriorly with its capsule against the gluteus minimus. On splitting the bone the tumor extended within 1.5 cm. of the articular surface of the acetabulum. The tumor tissue was composed of coarsely trabeculated osseous material with many blood-filled vascular channels (Fig. 3). Microscopic sections revealed an osteogenic sarcoma (Fig. 4).

The separately removed sacral biopsies also showed sarcoma.

Postoperatively his course was uneventful. Because of the question of an unsafe margin at the sacral border of transection, the patient received intensive roentgen radiation to this site as follows:

4000 r. in air through a 10 by 15 cm. field directly into the lateral sacrum. The total skin dose was 5200 r. given 200 r. daily with the following physical factors: 250 kv., 15 Ma, 0.5 mm. copper filter (H.V.L. 1.5 mm. copper).

He was discharged on crutches on April 28, 1948, and was fitted with a prosthesis (Fig. 5) in June, 1948. The patient, however, prefers to use his crutches. He is now completely rehabilitated and is employed as a registered pharmacist. Frequent checkup examinations and roentgenograms of the chest and pelvis have all been negative to date.

Fig. 2.—The left ureter and the bladder are pushed to the right by the tumor mass.

## COMMENT

The original diagnosis was made by Dr. Nathan B. Friedman and concurred in by Dr. Louis Lichtenstein and the Armed Forces Institute of Pathology (Acc. No. 207878). The latter suggested that the original tumor may have been a giant cell tumor which had become malignant.

Slides were sent in 1954 to Dr. Fred W. Stewart who made the diagnosis of telangiectactic osteogenic sarcoma.

## SUMMARY AND CONCLUSION

A seven-year survival of a patient with osteogenic sarcoma of the left ilium treated by hemipelvectomy is reported.

Fig. 4.




Fig. 3.

Fig. 3.—The tumor tissue on cross section was composed of coarsely trabeculated osseous tissue with many blood-filled vascular channels.
Fig. 4.—Shows irregular proliferation of atypical mesenchymal elements with formation of cartilage, osteoid and bony matrix.

Osteogenic sarcoma need not be considered as a contraindication for hemipelvectomy.

Because of the low surgical mortality and the excellent rehabilitation attainable with hemipelvectomy, this operation should be performed with increasing indications both palliatively as well as therapeutically.

Fig. 5.—Patient standing unassisted with aid of his prosthesis.

## REFERENCES

1. Bilroth, T., cited by Savariaud: Rev. Chir. **26:** 350, 1902.
2. Coley, Bradley L., Higginbotham, Normal L., and Romieu, Claude: Hemipelvectomy for Tumors of Bone, Am. J. Surg. **82:** 27, 1951.
3. Girard, C.: Rev. Chir. **18:** 1141, 1898.
4. Gordon-Taylor, G., and Wiles, P.: Interinnomino-abdominal (Hindquarter) Amputation, Brit. J. Surg. **22:** 671, 1935.
5. Pack, G. T., and Ehrlich, H. E.: Exarticulation of the Lower Extremities for Malignant Tumors. Part III. Sacro-iliac Disarticulation (Hemipelvectomy), Ann. Surg. **124:** 1, 1946.
6. Saint, J. H.: The Hindquarter (Interinnomino-abdominal) Amputation, Am. J. Surg. **80:** 142, 1950.
7. Taylor, G. W., and Rogers, W. P., Jr.: Hindquarter Amputation: Experience With Eighteen Cases, New England J. Med. **249:** 963, 1953.

# THE USE OF POLYETHYLENE TUBING TO RESTORE CONTINUITY IN SMALL ARTERIES

## Report of a Case

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*(From the General Surgical Service, Veterans Administration Medical Teaching Group Hospital)*

PERIPHERAL ischemia following crushing and avulsion injuries to an extremity may have two major causes. The first may be a mechanical obstruction of blood flow along normal arterial channels due either to injury to the vessel itself or to extrinsic pressure secondary to edema, hematoma, or displaced bony structures. The second cause is concomitant vasospasm which further diminishes the flow of blood through the uninjured collateral pathways. Obstruction and vasospasm in combination may produce severe ischemia in the limb distal to the site of injury so that survival of the extremity may be in doubt. Accepting the well-established fact that six hours of severe ischemia is tolerated by normal tissues and thereafter the chance of survival rapidly decreases, it becomes apparent that efforts during the early post-injury period must be directed toward relief of mechanical obstruction either by the restoration of continuity of the vessel or release of extrinsic pressure and control of vasospasm. Restoration of blood flow through a severed vessel need not be permanent in order to be of clinical value but may serve as a temporary channel until vasospasm can be controlled by an appropriate nerve block. Such a channel extends the "golden period" for relief of the ischemia and maintains the viability of the ischemic extremity during the period of maximal anoxia.

Injuries of the forearm and lower leg imply injuries to smaller arteries which are not amenable to grafting or primary suture because of the small luminal size. Polyethylene tubing, being an inert substance, may be used to temporarily bridge such an arterial defect. This has been used by Clatworthy and Varco,[1] and Schafer and Hardin[2] as a temporary arterial by-pass during the occlusion of major arteries and has been reported to function without thrombosis for short periods. The present report concerns the use of polyethylene tubing to restore continuity in a severed radial artery in a traumatized limb with loss of an undetermined number of collateral arterial pathways and severe vasospasm.

Received for publication Aug. 29, 1955.

## CASE REPORT

D. R. S., #100 377, a 19-year-old white man was admitted to the Veterans Administration Medical Teaching Group Hospital, March 11, 1953, for treatment of a compound fracture of the radius and ulna of the left arm with extensive loss of soft tissues of the forearm.

Four hours prior to admission, the patient's left forearm became impaled in the universal joint of a tractor. There was considerable blood loss. Following extraction of the arm, emergency first aid treatment was administered prior to evacuation to this facility.

Examination revealed a temperature of 98.6° F., pulse of 92, blood pressure of 156/85. The nail beds of the left hand were deeply cyanotic and the skin of the arm distal to the site of injury was blanched. There was no palpable radial pulse. A 10 inch, curvilinear laceration was present over the mid-portion of the dorsum of the forearm extending over the radial aspect to the ventral surface with extensive avulsion and maceration of the underlying tissues (Fig. 1). This involved a portion of the extensor and flexor elements

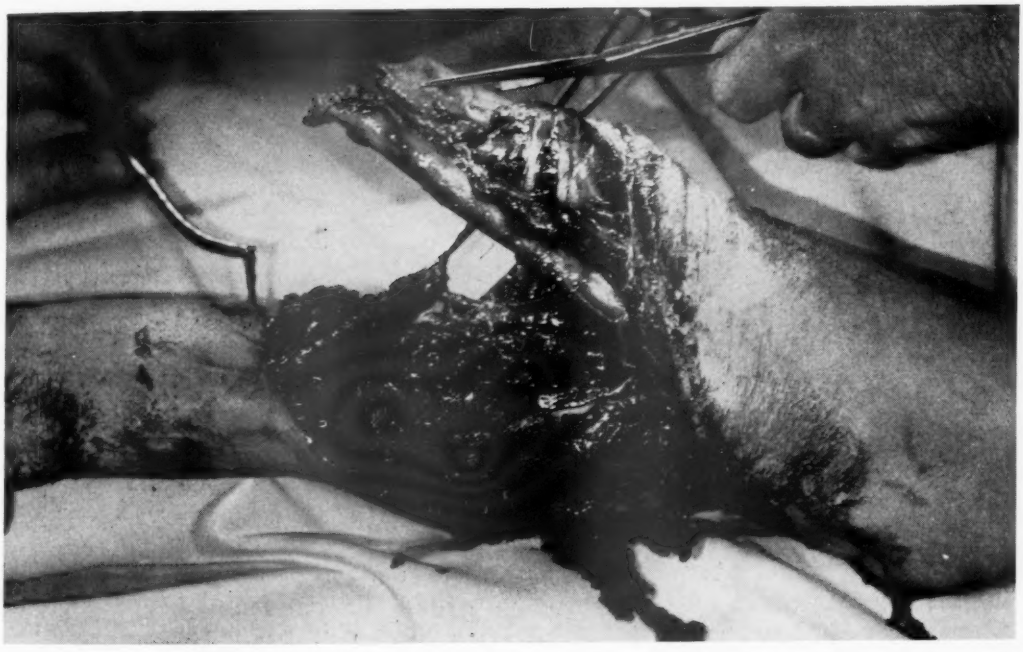

Fig. 1.—Photograph of the left forearm taken five hours after injury.

of the forearm in the region of the musculotendinous junction. There was a complete severance of the radial nerve. Compound comminuted fractures of the radius and ulna were present. The distal portion of the forearm and hand was connected to the proximal forearm by "a few intact flexor muscle bellies and a small bridge of ventral skin." In addition to the extensive muscular damage, a two and one-half inch segment of radial artery had been destroyed and both free ends of the severed artery could be identified. The ulnar artery could not be palpated in the intact volar muscles. Bleeding from the tissues distal to the site of injury was absent.

Six hours following injury, the patient was taken to the operating room and the forearm surgically prepared, scrubbed, and irrigated with large quantities of physiologic saline. It was noted that the proximal end of the radial artery had been occluded by a small clot. This was extracted with a resultant free flow of blood. The distal artery was patent. A two and one-half inch segment of polyethylene tubing, 0.066 inch in internal

diameter, was inserted into the proximal and distal ends of the severed artery and secured with 3-0 chromic catgut ligatures. Immediately thereafter, arterial pulsations reappeared in the distal artery. Within two minutes after insertion of the polyethylene graft, the hand which had been cold and blanched became pink and warm. The capillary pulse returned, and the cyanosis of the nail beds improved. Although pulsations could be felt in the artery distal to the shunt, no radial pulse could be palpated at the wrist. A radical débridement of the macerated muscles was performed, resulting in a large ventral soft tissue defect and the fractures of the radius and ulna were secured by internal fixation. A sterile dressing was applied and the arm immobilized. Following completion of the operation, a left stellate ganglion block was performed and repeated eight hours later. The color and warmth of the hand remained excellent although no radial pulsation was palpable. There was moderate edema of the distal limb. The wound healed satisfactorily being hastened by the application of split-thickness grafts sixteen days following injury.

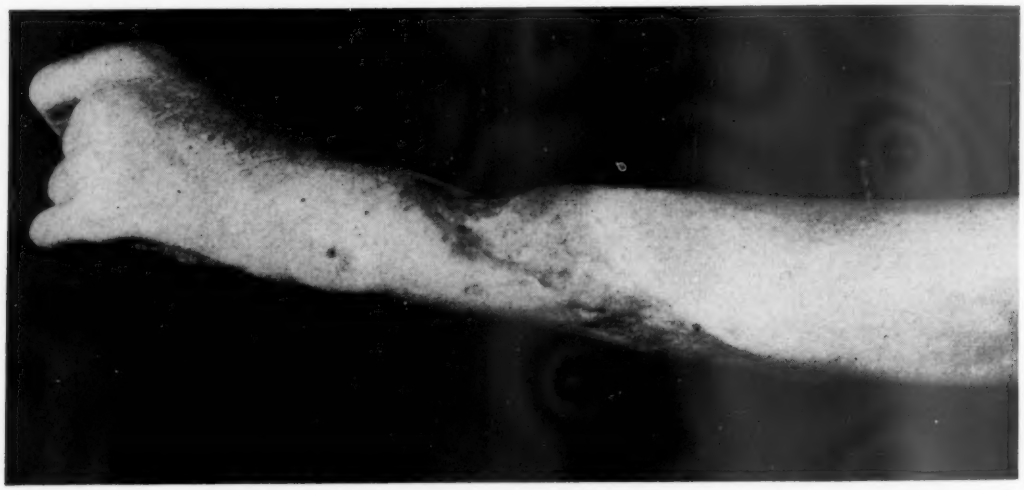

Fig. 2.—Appearance of left forearm six months following injury prior to rotation of pedical flap.

The patient was discharged on May 29, 1953, with the arm incorporated in a dorsal splint with rubber band traction to the fingers. He was readmitted on Aug. 18, 1953, and examination of the left arm revealed a one and one-half inch segment of exposed radius which appeared necrotic. A typical wrist drop and hypaesthesia were present over the dorsum of the hand secondary to the radial neuropathy. A weak radial pulse was reported at this time. On Aug. 31, 1953, a sequestrectomy was performed with removal of the exposed portion of the radius. At that time, the polyethylene tubing was visualized and removed. This was occluded. On Sept. 7, 1953, a small sequestrum of the ulna was removed. Final healing of the area was accomplished by the rotation of a full-thickness pedicle skin graft. He was discharged on Feb. 3, 1954, with the left arm incorporated in a cast. He returned on July 9, 1954, and at that time complete ankylosis of the left wrist was present with the fingers fixed in the claw position (Fig. 2). During this admission, a tendinous transfer procedure was performed. Daily physiotherapy was instituted and the patient was discharged on Sept. 10, 1954, with some improvement in function of the forearm.

## DISCUSSION

A regional sympathetic nerve block should be done at the time of initial observation in all cases of severe trauma to an extremity for relief of vasospasm. The orthopedic operating team had not recognized the possible benefit of stellate ganglion block in the early treatment of this case. When the

suggestion was made, the anesthetist thought it unwise to perform the regional block because general anesthesia had already been induced. Therefore, vasospasm persisted, and the distal forearm, six hours after trauma, was white, pulseless, and showed little bleeding from the traumatized tissues. It was the opinion of most observers that there was little chance of salvage of the distal extremity. The restoration of the radial artery by the insertion of the polyethylene shunt resulted in the immediate return of both warmth and color to the distal extremity. The pulse became palpable in the radial artery distal to the shunt although the radial pulse at the wrist was not felt. The circulation was visibly enhanced by the shunt prior to control of vasospasm by nerve block. It was not possible to determine the time when the shunt occluded postoperatively because no significant change occurred in the circulatory status. It was our opinion that the chances of survival of the distal extremity had been enhanced by the polyethylene shunt in the radial artery. This suggests that it would be a useful adjunct procedure in the future to correct posttraumatic extremity ischemia due to injuries involving small arteries.

## REFERENCES

1. Clatworthy, H. W., and Varco, R. L.: A Small Bore Polythene Shunt to Prevent Mechanical Shock After Prolonged Cross-clamping of the Thoracic Aorta, Proc. Soc. Exper. Biol. & Med. 74: 434, 1950.
2. Schafer, P. W., and Hardin, C. A.: The Use of Temporary Polythene Shunts to Permit Occlusion, Resection, and Frozen Homologous Graft Replacement of Vital Vessel Segments, SURGERY 31: 186, 1952.

# Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

## ARTERIAL THROMBOSIS ASSOCIATED WITH CERVICAL RIBS: SURGICAL CONSIDERATIONS

### REPORT OF A CASE AND REVIEW OF THE LITERATURE

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THE vascular complications of cervical ribs are not common. When present they range from postural obliteration of arterial pulsations to arterial thrombosis with associated gangrene. Although the cervical rib, the initiating cause of vascular complications, is at the level of the subclavian artery, the vascular pathology is not always limited to this arterial segment alone. A review of the literature reveals that, in most cases, the vascular lesions are found at all levels of the arterial tree including and distal to the subclavian artery. The use of angiography for exact localization of the lesions and of arterial grafts for the restitution of vascular continuity may offer a more rational approach to the solution of this problem.

A review of the literature, which has revealed only 29 cases, is presented for the evaluation of both the clinicopathologic manifestations and the methods of treatment. The relative infrequency of arterial thrombosis associated with cervical ribs has prompted the report of a case which appears to illustrate the major aspects of this problem. This case is the first one in which vascular continuity was restored by arterial grafting.

#### CASE REPORT

*History.*—P. C. (No. 71193), a 32-year-old, right-handed, white, female social worker, was admitted to the Montefiore Hospital in February, 1955, complaining of weakness, pallor, and coldness of the right hand. She dated the onset of these symptoms to a bus accident six months previously, at which time she was lurched out of her seat and hit her right shoulder against a seat rail guard. Three weeks after the accident she noted tingling in the right fourth and fifth fingers. These symptoms, initially intermittent, became progressively worse and came to be associated with pallor, increasing pain, weakness, and easy fatigability of the hand.

*Physical Examination.*—On admission to the hospital, the abnormal physical findings were limited to the right upper extremity. There was a tender mass in the supraclavicular

Received for publication Nov. 23, 1955.

fossa; this mass did not pulsate and there was no bruit over it. The skin of the hand and forearm was cold and moist. The grip was weak and the hand became cadaverically white with exercise. Exercise tolerance on the right was diminished. No pulsation could be felt in the subclavian, axillary, brachial, radial, or ulnar arteries. The oscillometric and skin temperature readings appear in Tables I and II. There was no muscle atrophy or other trophic changes.

*X-ray.*—Roentgenographic studies revealed bilateral cervical ribs; the right was a complete one forming a joint with the axillary portion of the first rib (Fig. 1). An angiogram, using the Fairchild camera, was performed for localization of the arterial block. Fifty cubic centimeter of 70 per cent Urokon was introduced into the left antecubital vein and a series of films taken. Opacification of the innominante, right vertebral, and axillary arteries was obtained at nine seconds. The subclavian artery beyond the vertebral branch was not opacified (Fig. 2).

The clinical evidence of severe progressive ischemia and the radiographic demonstration of segmental subclavian artery occlusion constituted the indication for surgery.

TABLE I. SKIN TEMPERATURES

| FINGER | LEFT | RIGHT | |
|---|---|---|---|
| | | PREOPERATIVE | POSTOPERATIVE |
| 1 | 91.5 | 76.0 | 90.0 |
| 2 | 87.0 | 74.1 | 83.0 |
| 3 | 89.5 | 75.7 | 86.5 |
| 4 | 88.0 | 77.5 | 87.0 |
| 5 | 87.5 | 79.2 | 90.5 |
| Thenar | 90.5 | 87.8 | 92.0 |
| Hypothenar | 91.0 | 88.0 | 91.0 |

TABLE II. OSCILLOMETRIC READINGS

| | LEFT | RIGHT | |
|---|---|---|---|
| | | PREOPERATIVE | POSTOPERATIVE |
| Upper arm | 3.5 | 0.0 | 1.5 |
| Antecubital | 2.5 | 0.0 | 1.0 |
| Wrist | 1.0 | 0.0 | 0.2 |

*Operation.*—The patient was positioned so as to obtain abduction of the right arm and hyperextension of the cervical and upper dorsal spine. Endotracheal anesthesia was utilized. A skin incision was made directly over the clavicle with a T-limb directed toward the intertubercular sulcus of the humerus. The platysma was mobilized with the skin flaps. The middle third of the clavicle was resected subperiosteally and the humeral attachment of the pectoralis muscle was reflected medially. After retracting the phrenic nerve, the scalenus anterior was divided through its tendinous insertion and one centimeter of normal muscle was resected. Complete exposure of the cervical subclavian artery and proximal axillary artery was obtained. There was a thrombotic occlusion of the third part of the subclavian with normal artery proximally and distally. The thrombotic segment measured 3.2 cm. in length and exhibited a slight fusiform dilatation about the thrombus. The thrombosed segment was densely adherent to the surrounding structures (Fig. 3). No significant collateral arterial circulation was encountered and there were no prominent venules. The anterior portion of the cervical rib was disarticulated and the rib resected to the site of the transverse process. A bull-dog clamp was applied distal to the thrombus before the actual handling of the artery. Thromboendarterectomy was performed, but resection and homologous graft replacement seemed to offer a more satisfactory means of reconstituting the blood flow. A homologous iliac artery graft preserved in a nutrient solution, was utilized. The axillary artery was isolated distal to the superior thoracic branch. A proximal bull-dog clamp was applied just beyond the thoracoacromial axis. An anastomosis was performed using 5-0 continuous everting silk sutures. At the completion of the implantation there was a vigorous

Fig. 1.—An oblique view demonstrates the complete right cervical rib.

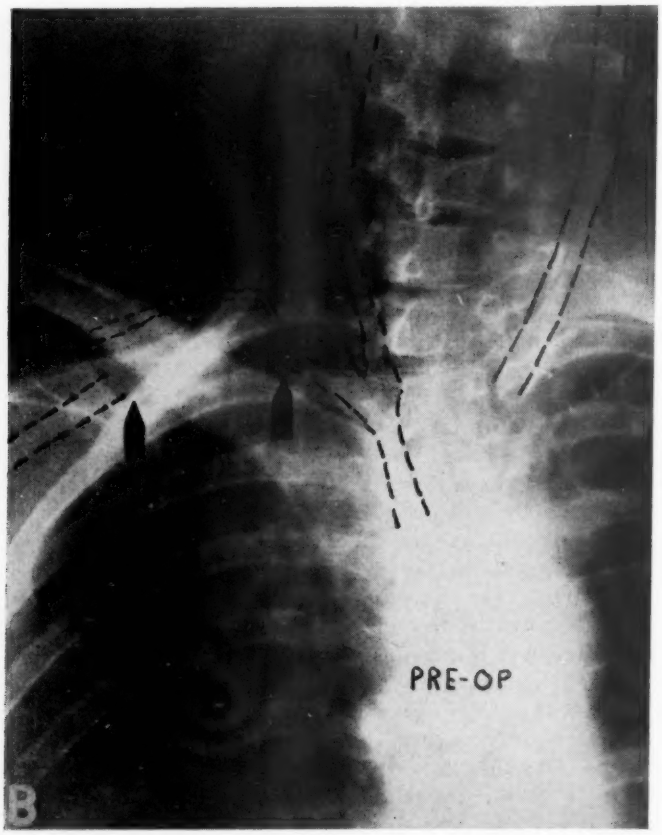


Fig. 2.—The retouched angiogram, taken nine seconds after intravenous injection, demonstrates the site of arterial block. No collateral circulation is demonstrated.

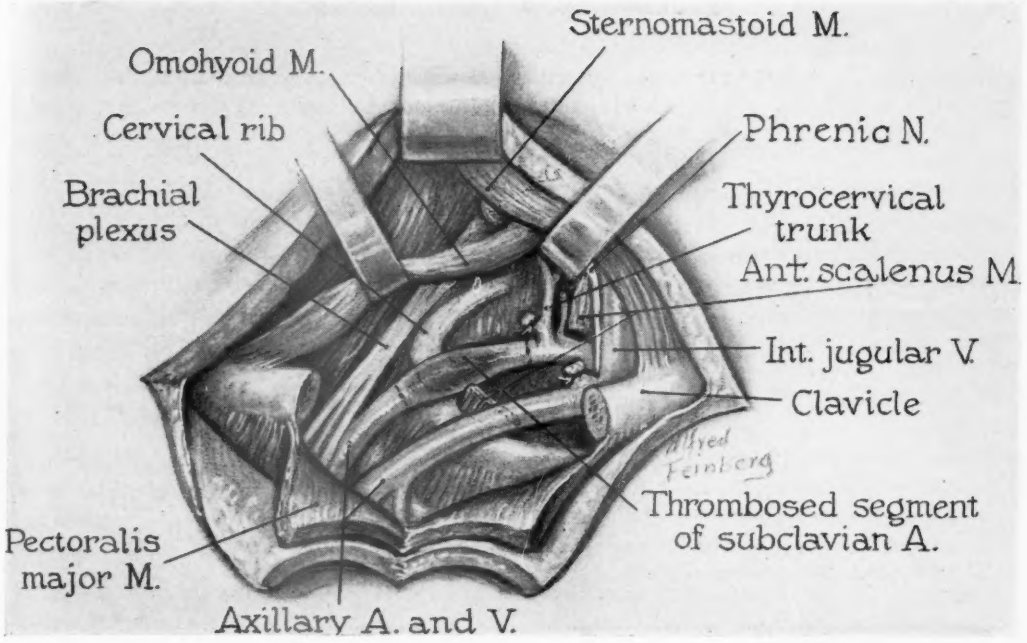


Fig. 3.—Diagram of the operative findings as seen after resection of the middle third of the clavicle and resection of the scalenus anticus. The relations of the cervical rib to the site of subclavian thrombosis is depicted. The dotted line on the artery indicates the site of arterial resection.

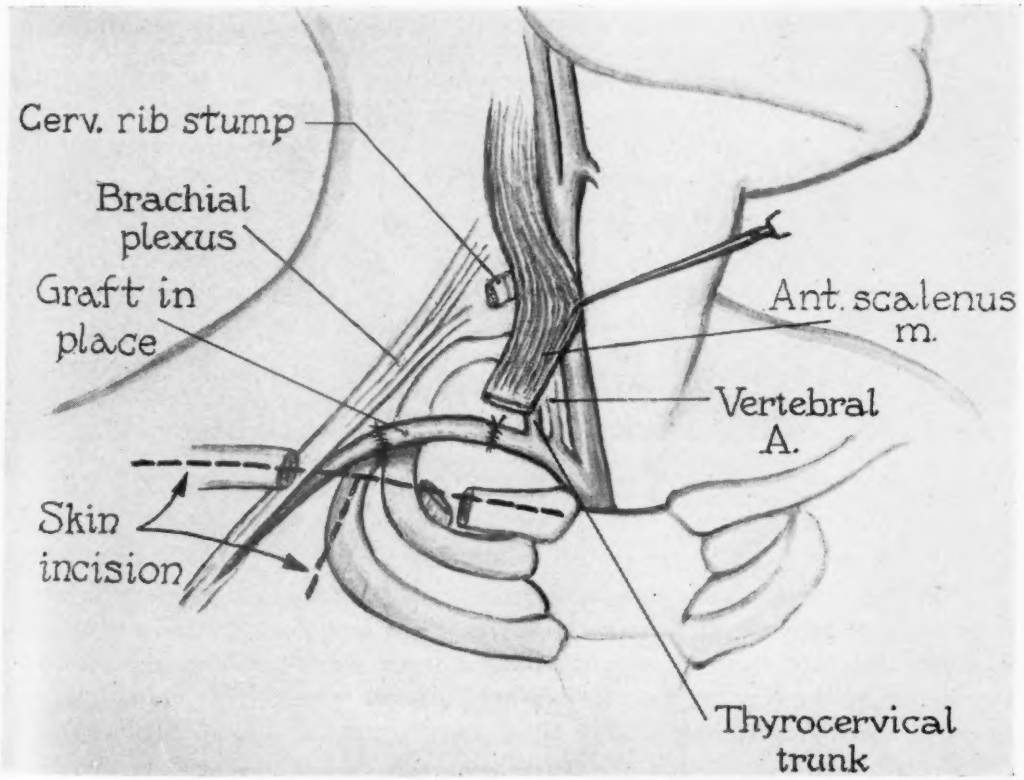


Fig. 4.—Diagram of the extent of the operative procedure. The dotted line indicates the skin incision over the resected clavicle and its perpendicular extension for exposure of the axillary artery. The divided and resected scalene muscle is retracted to demonstrate the posterior stump of remaining cervical rib. The length and position of the arterial graft is shown.

pulsatile flow through the graft and the axillary artery (Fig. 4). The pectoralis muscle was reconstituted and the wound closed in layers without drainage. A continuous procaine stellate ganglion block was maintained for twenty-four hours. The postoperative course was uneventful.

*Pathology.*—The resected rib was 5.8 cm. in length. The resected artery measured 3.5 × 2.0 × 0.7 cm.; its lumen was completely occluded by an organized thrombus; there was normal arterial wall on each side of the thrombus. Microscopic examination revealed focal intimal ulceration with a firmly attached thrombus; the subintima was thickened. The adventitia was markedly thickened by the fibroplastic proliferation and foci of granulation tissue. These findings are consistent with segmental arterial thrombosis and marked adventitial fibrosis.

*Results.*—The ulnar hypesthesia disappeared immediately. There was immediate evidence of increased vascularity. The skin became warm, and a pulse could be felt in the brachial artery. There was no return of wrist pulses nine months postoperatively. Muscle power and exercise tolerance returned to normal. There was no limitation of shoulder girdle function and the clavicular resection had created no deformity (Fig. 5). The patient still notes slight blanching of the fingers on exposure to cold. Nine months after the operation, this constitutes her sole complaint.

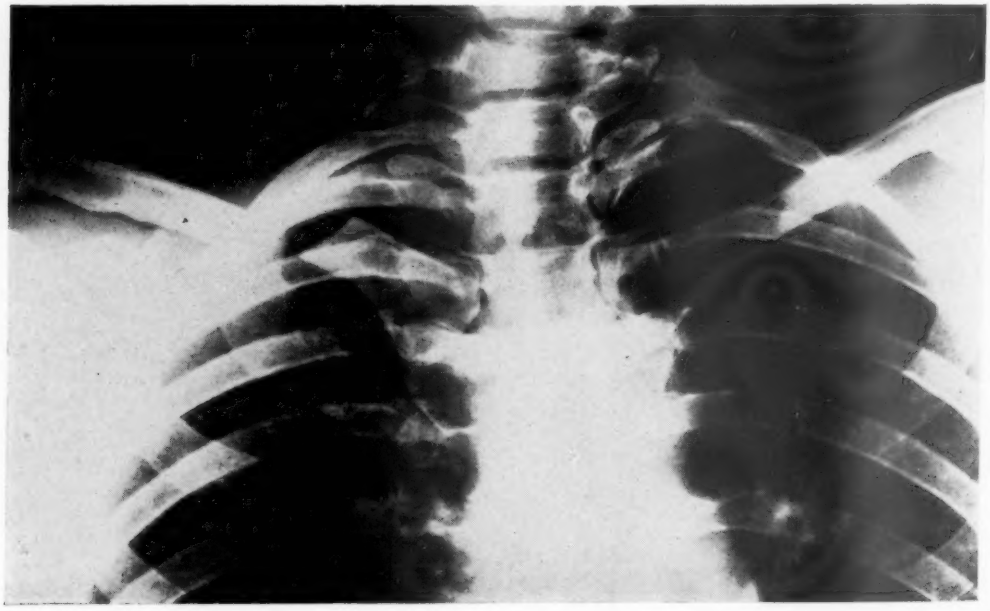

Fig. 5.—A postoperative roentgenogram showing the extent of the clavicular resection and of the cervical costectomy.

## REVIEW OF THE LITERATURE

Table III summarizes the published cases of thrombosis of the subclavian artery in association with cervical rib. This study includes only those cases with adequate data necessary to establish the diagnosis and to evaluate the course of the disease or the results of its treatment. In some reports it is difficult to distinguish between thrombosis, true aneurysm formation, and constriction associated with poststenotic dilatation. Wilson and Bruce[61] point out that there is a good deal of warranted skepticism about many of the subclavian aneurysms associated with cervical ribs. It should be also pointed out that in some cases the elliptical dilatation of the subclavian artery associated with cervical ribs

may simulate a fusiform aneurysm with secondary thrombosis. However, as indicated by Lindskog,[36] this type of "aneurysm" does not tend to increase in size nor exhibit the usual aneurysmal complications of enlargement or rupture. It is likely that some early reports on this subject deal with thrombosed subclavian arteries somewhat elliptical shaped rather than with true aneurysms. Keen in 1907[27] and Murphy in 1906[42] had already commented on this point and stressed such diagnostic difficulties. True aneurysms are seen very infrequently as indicated by Adson.[1] The cases of Fischer,[17] Grisson,[20] Imler and associates,[25] and Mac Fee[40] appear to illustrate this point. For the purposes of this review, in order to avoid any confusion, the cases labeled as "aneurysms" with or without thrombosis are not tabulated.

Likewise, the vascular disorders associated with osseus abnormalities of the thoracic outlet not primarily due to cervical ribs are excluded. Such experiences have been reported by Adson and Allen,[2] Bricker,[10] Eden,[14] Henschen and Heusser,[22] Walshe and associates,[56] and Russel.[49]

A certain number of published cases of cervical ribs associated with various degrees of arterial insufficiency could not be tabulated because of inadequate information concerning the status of the blood vessels. For this reason we have excluded the cases of Keen,[27] Willet,[60] Chiari,[32] and Gordon.[19] Matas[39] mentions a case of traumatic subclavian thrombosis caused by "impaction, contusion of the artery on the tip of the projecting cervical rib"; but there are no further details. Jacobsohn[26] reviewed 554 cases of cervical ribs and mentioned six with gangrene; no details are reported. Adson's review[3] comments on two cases with calcareous deposits in the wall of the subclavian artery at the site of obstruction. One of these had gangrene of the finger and died during surgery of hemorrhage from the diseased vessel.

The following analysis of the clinicopathologic manifestations concerns itself only with the cases of arterial thrombosis. From this series of 30 cases certain facts merit particular emphasis.

The patients ranged in age from 16 to 66 with 73 per cent falling into the 21 to 50 age group. Eighteen were men and 12 women. Eighteen occurred on the right side and 11 on the left. Thus, 60 per cent of cases occurred in men, and 60 per cent were on the right side in both sexes. The cervical rib, except in one case, was a complete one in all the instances in which this information could be obtained. The contralateral rib was usually as well developed as that on the symptomatic side. Coote's case[12] is reported as being associated with an exostosis of a cervical rib. Information regarding the relationship between handedness and side involved is not available.

A supraclavicular mass, present in all patients, was represented by the palpable rib, the displaced artery, and the periarterial inflammatory reaction. The mass was occasionally tender. A bruit was audible when the occlusion was only partial and disappeared when the arterial occlusion became complete.[15]

A traumatic incident often preceded the appearance of symptoms. Sometimes this was represented by small traumata of an occupational nature associated with carrying objects. Often the symptoms of acute vascular insufficiency were initiated by a single incident, such as a blunt force blow or an unusually strenuous muscular effort.

TABLE III. SUMMARY OF CASES PRESENTING ARTERIAL THROMBOSIS IN ASSOCIATION WITH CERVICAL RIBS

| AUTHOR | AGE | SEX | SIDE | NEUROLOGIC SYMPTOMS | VASCULAR SYMPTOMS | TREATMENT | RESULTS |
|---|---|---|---|---|---|---|---|
| Hodgson[23] 1815 | 53 | M | L | ? | All pulses absent; gangrene of phalanx | Poultices | Pulses did not return; less cold |
| Copper[11] 1818 | ? | F | ? | ? | Absent wrist pulses; "gangrenous spots" | "Warmth and friction"; "pressure on subclavian" | Pulses did not return; improved |
| Coote[12] 1861 | 26 | F | L | + | No pulses; cold | Costectomy | Pulses did not return; improved |
| Ehrich[16, 53] 1895 | 22 | F | L | + | No pulses; vasomotor | Costectomy | Pulses did not return; improved |
| Billington[9] 1905 | 42 | F | L | 0 | No radial pulse; cold; pallor | Excision of thrombosed segment | Pain disappeared |
| Babcock[5] 1916 | 22 | M | R | ? | Absent wrist pulses; gangrene of digits; atrophy of arm | Costectomy | Pulses returned; marked improvement |
| Benedik[8] 1924 | 38 | F | R | 0 | No arm or wrist pulses; gangrene of digits | Scalenotomy; costectomy | Improved, but remained with poor motor power and persistent vasomotor changes |
| Otto[45] 1924 | 57 | F | R | + | Gangrene of digits | 0 | Autopsy revealed thrombosis in subclavian artery and also one in the radial artery |
| Symonds[54] 1927 | 29 | F | R | + | No wrist or arm pulses | 0 | Proximal extension with hemiplegia |
| | 20 | F | R | 0 | No wrist or arm pulses | 0 | Proximal extension with hemiplegia |
| Oljenick[44] 1929 | 24 | F | L | 0 | No pulses; cold; vasomotor changes | Scalenotomy | Remained with poor exercise tolerance, coldness, vasomotor changes; pulses returned in four months |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Langeron and Desbonnets[30] 1931 | 26 | M | L | ++ | No pulses; cold; discoloration of hand and forearm; ulceration of finger | Costectomy; resection of thrombosed segment | Improved progressively |
| Langeron, Tierny, and Paris[31] 1931 | 66 | M | R | 0 | No pulses; vasomotor changes | Resection of artery | Pulses did not return; pain disappeared; color improved |
| Leriche[33] 1935 | 48 | F | L | 0 | No wrist or arm pulses; Raynaud's | Costectomy | Pulses did not return; five years later the subclavian pulse disappeared |
| | 45 | M | R | 0 | No wrist pulses; brachial pulse small; cold; vasomotor changes | Costectomy; periarterial (brachial) stripping | Oscillometrics improved |
| Picot[48] 1935 | 34 | M | R | + | Absent wrist and arm pulses; vasomotor changes; gangrene of fingers | Scalenotomy; costectomy | Radial pulses did not return; oscillometrics in arm improved; vasomotor changes less marked |
| Sénèque and Lelong[50] 1935 | 16 | F | R | + | Oscillometrics in wrist and arm markedly decreased; vasomotor changes; loss of motor power | Costectomy; periarterial stripping. Resection of thrombosed brachial artery | No significant improvement |
| Wertheimer[58] 1935 | 50 | F | R | 0 | No wrist or arm pulses | Resection of thrombosed artery | Preoperative arteriogram showed block at the axillary artery; no return of pulses; vasomotor changes persisted |
| Flint[18] 1937 | 45 | F | R | 0 | No pulses; cyanosis; atrophy | Scalenotomy; resection of thrombosed artery | Improved |
| Baumgartner, Clerc, and Macrez[7] 1938 | 24 | F | R | + | No wrist or arm pulses; cold; infected gangrene | Costectomy; resection of thrombosed artery | Good |
| Lenner[32] 1938 | 35 | M | R | 0 | No wrist or arm pulses; gangrene of forearm | Major amputation | |
| Eden[14] 1939 | 57 | F | L | 0 | No pulses | Scalenotomy; costectomy | No return of pulses |

TABLE III.—CONT'D

| AUTHOR | AGE | SEX | SIDE | NEUROLOGIC SYMPTOMS | VASCULAR SYMPTOMS | TREATMENT | RESULTS |
|---|---|---|---|---|---|---|---|
| Donald and Morton[13] 1940 | 32 | M | L | 0 | Gangrene of hand and forearm | Major amputation; scalenotomy; costectomy | Brachial pulse returned |
| Patterson[46] 1940 | 28 | F | L | + | No pulses | Scalenotomy; costectomy | Improved; numbness persists |
| Silbert[51] 1940 | 38 | F | L | 0 | Pulses absent beyond axillary; cold; Oscillometric arm-faint forearm-O | Costectomy | Pulse returned two and one-half months postoperative |
| Hoobler[24] 1942 | 38 | M | R | ? | All pulses disappeared sequentially | Scalenotomy | Hemiplegia later; persistent symptoms |
| Luke and Fountain[38] 1950 | 51 | M | R | + | Vasomotor changes; trophic changes | Scalenotomy; costectomy; dorsal sympathectomy | Improved; the involved finger remained cold, due to digital thrombosis |
| Petronio[47] 1952 | 60 | F | R | 0 | No pulses; gangrene of digits | Scalenotomy; costectomy; thrombectomy | Pulses did not return; improved |
| Lord[37] 1955 | 44 | F | R | ? | Raynaud's; thrombosis of subclavian artery and vein | Scalenotomy; claviculectomy | Pulses returned; cervical rib with hyperabduction syndrome |
| Schein, Haimovici and Young 1955 | 32 | F | R | 0 | Vasomotor changes; marked ischemia; third portion of subclavian not palpable | Scalenotomy; costectomy; resection of subclavian artery with homologous graft replacement | Brachial pulse returned; marked improvement |

Associated brachial plexus involvement was noted in 9 patients. In such cases the symptoms represented a minor feature in the clinical picture and in no case were they distressing. It was not always possible to distinguish accurately between the ischemic and neuritic origin of pain. In all patients operated upon, the neurologic manifestations disappeared promptly and permanently following release of any one of the walls of the supraclavicular region. Such improvement was not always paralleled by beneficial changes in vascular symptomatology.

The vascular symptoms consisted of pain, pallor, paresthesias, coldness, vasomotor phenomena, decreased exercise tolerance, muscle weakness, and trophic changes. Eleven patients (36.7 per cent) sustained a loss of a phalanx or a digit, and two (6.7 per cent) required major upper extremity amputations. In three patients proximal extension of the subclavian thrombosis resulted in involvement of the common carotid artery with contralateral hemiplegia. The disease may be initiated dramatically with early peripheral ischemia and gangrene.[31, 32] More commonly, the vascular symptoms appeared as peripheral arterial spasm without loss of pulsations, or with ulnar or radial artery occlusion without trophic changes. The cervical rib as a cause of subclavian artery occlusion was sometimes undiagnosed until advanced trophic changes had taken place.

The majority of operative procedures were directed at releasing the subclavian artery by scalenotomy or cervical costectomy.

Twenty-four patients were operated upon. The procedures performed appear in Table III, and comprise 17 cervical costectomies, 12 scalenotomies, and 7 arterectomies of the thrombosed arterial segments. Periarterial stripping, dorsal sympathectomy, thrombectomy, and arterial graft replacement were each performed once. No patient became worse following surgical therapy, regardless of the type of procedure performed. Likewise, all were promptly relieved of neuralgic symptoms. Except for the 2 patients requiring major amputations, digital trophic changes healed in all cases, without further progression of the gangrenous process.

The operative results were completely satisfactory in the 4 patients in whom a return of wrist pulses was achieved. The results were functionally satisfactory in the 5 additional patients in whom there was a return of brachial pulsations. The postoperative reappearance of pulsations distal to the subclavian artery is of prognostic significance in evaluating the surgical result. Where this was not achieved the patients remained with significant limiting vascular impairment characterized by decreased motor power, exercise tolerance, and persistent vasomotor changes. In this latter group of cases, it is likely that the residual manifestations of arterial insufficiency can be ascribed to the occlusion of the brachial artery or its branches. In the face of persistent and disabling manifestations, increase of collateral circulation by the use of sympathetic denervation may be indicated. Continuous stellate ganglion blocks repeated as often as is necessary or even a sympathetic ganglionectomy should be considered.[4, 33, 55]

## DISCUSSION

Cervical ribs are encountered in 0.5 to 0.7 per cent of routine chest films.[59] The vast majority of these patients are asymptomatic. The largest group of

symptomatic patients are those with impingement upon the brachial plexus by an incomplete cervical rib. Adson[1] reported vascular symptoms in 5.6 per cent of patients. These are manifested as Raynaud's phenomenon or with signs referable to partial intermittent subclavian artery occlusion. Arterial thrombotic complications are relatively uncommon.

The presence of a complete cervical rib (Gruber's classifications 3 and 4) is associated with a significant alteration in the cervical course of the corresponding subclavian artery.[21] A complete cervical rib represents a superior extension of the costal cage. In its course through the thoracic outlet the artery must course higher in the neck, closer to the midline and more anteriorly than normally. It must angulate when passing over the cervical rib. Furthermore, the anterior-posterior support of the normal artery is represented by the scalenus anterior and the first rib. This space is narrowed by the presence of an intervening complete cervical rib into a viselike slit. Clavicular resection, in the present case, was carried out for improved surgical exposure. However, LeVay[34] and McGowan[41] have indicated that the clavicle may also contribute to the vise mechanism that results in subclavian artery occlusion. Scalenotomy serves only to allow more space anteriorly without altering either the increased vertical ascent or the exaggerated curve of the artery. Cervical costectomy combined with scalenotomy allows the artery to fall into a normal position. Vascular symptoms are unlikely to occur when the cervical rib is incomplete because the course of the artery is not altered and there is no anteroposterior compression. For the same reason an incomplete cervical rib is more likely to involve only the more posterior and inferiorly placed lower cord of the brachial plexus. Radiographic demonstration of the length of a symptomatic cervical rib may aid in the differentiation between the neurologic and ischemic origin of symptoms.

The existing anatomic condition may be aggravated by associated static or postural abnormalities such as sloping shoulders, scoliosis, varying degrees of shoulder girdle development, and anomalies or fracture deformities of the cervical vertebra, clavicle, or first rib. Certainly symptomatic vascular "scalenus anticus syndromes" have been described without cervical ribs, in association with anomalies of the first rib or a hypertrophied scalenus anticus muscle.[43, 52] Such vascular complications have been sufficiently severe to have resulted in gangrene. Narrowing of the base of the subclavian triangle by the Adson maneuver or by carrying a weight on the affected side may bring about a diminution in pulses and oscillometric readings in the corresponding radial artery of the completely asymptomatic patient. When this phenomenon is repeatedly reversible it is probably of no significance. It is conceivable that trauma to the neck in a patient with an anatomic anomaly may produce significant changes. Such changes have also been observed as a result of hemorrhage into the supraclavicular fossa, with resultant external arterial compression.[6]

There is no reasonable explanation for the unilaterality of vascular involvement in the face of bilateral cervical ribs of equal length, except for the role of trauma.

Trauma in the susceptible individual may be due to no more than the use and abuse occurring within the normal range of shoulder girdle function. Thrombosis of the artery is localized and occurs as a result of local intimal changes. This intimal injury if not primarily caused by is related, at least in part, to actual cervical vascular trauma. Localized calcareous plaques at the point of cervical rib compression have been described and may constitute the prethrombotic stage of the disease. The structural changes in the arterial wall that precede thrombus formation may occur as a result of direct contusion of the major vessel. Dense adhesions of the thrombotic segments to the surrounding structures have also been observed by Langeron,[30] Eden,[14] and Leriche.[33]

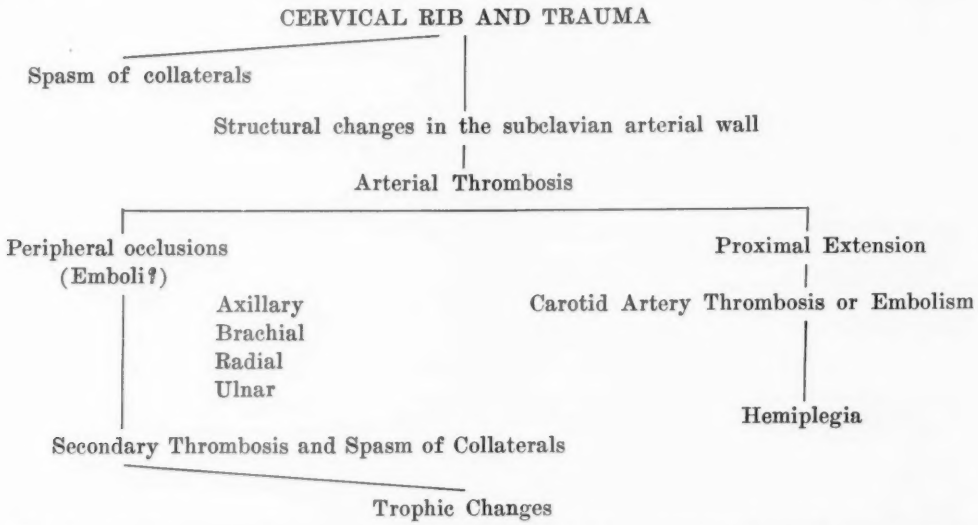


Fig. 6.— A diagrammatic representation of the probable sequence of events occurring in the arterial system exhibiting significant vascular changes associated with cervical rib disease.

It is also possible for arterial changes to occur as a result of prolonged and continuous arterial spasm initiated by direct contact between the artery and the cervical rib. The initial thrombus may be small and insufficient to occlude the subclavian artery. However, such a thrombus may embolize to one of the more peripheral vessels and serve as a second site of arterial occlusion, with associated spasm of the collateral system of the occluded artery.[35] The sequence of embolic occlusion and secondary thrombosis with reflex vasospasm of collaterals may occur throughout the distal arterial tree. This sequence of events explains why the wrist and arm pulses may be absent, and trophic changes occur in the presence of a normal subclavian pulsation. The subclavian artery may also become progressively occluded. This sequence of events has been observed in the cases described by Otto,[45] Leriche,[33] and Hoobler.[24]

Proximal extension of the thrombus results in involvement of the ipsilateral carotid artery. It becomes apparent that although scalenotomy and cervical costectomy return the artery to a normal position and remove the compressive factor, the remaining thrombus may constitute a continuing threat to the collateral circulation. A rational surgical therapy, therefore, should include removal of the thrombosed arterial segment.

The vascular complications associated with cervical ribs may be classified according to the stage of the disease: (1) Compression of the subclavian artery without ischemia; (2) compression of the subclavian artery with ischemia; (3) peripheral arterial occlusion without apparent subclavian artery thrombosis; (4) subclavian artery thrombosis, incomplete and complete; (5) subclavian artery thrombosis with peripheral arterial occlusions; and (6) each of the above with trophic changes.

Once thrombatic occlusion of the subclavian artery has occurred the survival of the extremity depends upon the collateral circulation. In most cases the collateral circulation between the first part of the subclavian and the first and second parts of the axillary artery is ample. However, in 3 of the tabulated cases the thrombus extended proximally to involve the first part of the subclavian artery. The collateral circulation is represented by the transverse cervical, transverse scapular, and costocervical branches of the subclavian artery anastomosing with the thoracoacromial, subscapular, and anterior and posterior humeral circumflex branches of the axillary artery. This collateral circulation is usually adequate, but not predictably so. Even in the extremity that has no vascular disease, acute interruption of the subclavian artery has occasionally been followed by vascular insufficiency of the arm. Gangrene of the forearm has been reported four times following pulmonary-subclavian anastomosis performed for tetralogy of Fallot,[29, 57] and once when a subclavian artery was used for the reconstruction of a coarctation of the aorta.[28] The situation, though not directly comparable, indicates the degree of variability of the collateral circulation. The patient with a thrombus of the subclavian artery who has signs of vascular insufficiency obviously has an inadequate collateral circulation. This may be the result of one or more arterial occlusions of the extremity. Spontaneous improvement occurring as the result of recanalization is unpredictable.

There is a high incidence of persistent postoperative vascular insufficiency regardless of the procedure used. The surgical management should aim at correcting the anatomic-pathologic disturbances. As a first step it is possible to restore the vessel to its normal position and remove the compressive and irritative focus by scalenotomy and cervical costectomy. Resection of the thrombosed arterial segment is necessary in order to remove the focus of reflex vasoconstrictive impulses[33] and to allow for the reconstitution of blood flow by grafting. A combination of these methods would appear to hold the greatest promise for restoration of normal limb function.

## SUMMARY

1. The clinical and pathologic manifestations resulting from subclavian arterial thrombosis associated with cervical ribs in 30 cases have been reviewed.

2. Trophic changes ranging from minor to massive gangrene of the upper extremity were present in 43.3 per cent of these cases.

3. Review of the literature indicates that, regardless of the surgical procedure performed, significant residual manifestations of vascular insufficiency were present, if restoration of pulsations below the subclavian artery was not achieved.

4. The cause of the residual vascular manifestations after surgery can be ascribed in most cases to occlusive arterial disease affecting the arterial tree distal to the subclavian artery.

5. Preoperative evaluation of the entire arterial tree of the involved upper extremity by arteriography is suggested as it may be valuable in the surgical management.

6. The operative procedure should aim (a) at restoring the subclavian artery to its normal anatomic position, and (b) at re-establishing the arterial flow to the upper extremity. Scalenotomy, costectomy, and claviculectomy either singly or in combination may be adequate in some cases. Resection of the thrombotic subclavian artery and restoration of vascular continuity by grafts should be used whenever possible. Sympathetic denervation of the upper extremity may be necessary to promote collateral circulation if multiple distal arterial occlusions are present.

7. The suggested comprehensive plan of surgical management of arterial thrombosis associated with cervical ribs is based upon the concept that the arterial occlusion may affect several levels of the involved extremity. An illustrative case report is presented.

The authors wish to thank Mr. Alfred Feinberg for the drawings, and Mr. Antol H. Herskovitz, medical photographer, for his film of this case and of the surgical procedure performed.

## REFERENCES

1. Adson, A. W.: Surgical Treatment of Symptoms Produced by Cervical Ribs and the Scalenus Anticus Muscle, Surg., Gynec. and Obst. **85**: 687, 1947.
2. Adson, A. W., and Allen, E. V.: Thrombosis of Arteries of the Right Upper Extremity Resulting from Anomalous First Rib, Proc. Staff. Meet., Mayo Clin. **13**: 637, 1938.
3. Adson, A. W., and Coffey, J. R.: Cervical Rib. A Method of Anterior Approach for Relief of Symptoms by Division of Scalenus Anticus, Ann. Surg. **85**: 839, 1927.
4. Allen, E. V., Barker, N. W., and Hines, E. A., Jr.; Peripheral Vascular Diseases, ed. 2, Philadelphia, 1955, W. B. Saunders Company, p. 175.
5. Babcock, W. W.: Cervical Rib With Resulting Gangrene of the Fingers, Am. Med. **10**: 616, 1916.
6. Basset, R. C.: Brachial Plexus and Subclavian Artery Embarrassment Caused by Hemorrhage into the Supraclavicular Fossa, SURGERY **31**: 750, 1952.
7. Baumgartner, A., Clerc., A., and Macrez, C.: Sur L'anévrysme Artériel de Voisinage et la Gangrène Ischémique des Doigts en Rapport Avec les Côtes Cervicales. Leur Traitement Chirurgical, Presse Méd. **46**: 1665, 1938.
8. Benedik, L.: Raynaudscher Symptomkomplex Bei Halsrippe, Deutsche Ztschr. Nervenh. **82**: 217, 1924.
9. Billington, W.: Excision of Subclavian Aneurysm Associated With Cervical Rib, Brit. J. Surg. **19**: 334, 1931.
10. Bricker, W. M.: Brachial Plexus Pressure by the Normal First Rib, Ann. Surg. **85**: 558, 1927.
11. Cooper, A. P., and Travers, B.: Surgical Essay (London) **1**: 173, 1818.
12. Coote, H.: Pressure on the Axillary Vessels and Nerve by an Exostosis from a Cervical Rib. Interference With the Circulation of the Arm. Removal of the Rib and Exostosis. Recovery, Med. Times & Gazette **2**: 108, 1861.
13. Donald, J. M., and Morton, B. F.: The Scalenus Anticus Syndrome With and Without Cervical Rib, Ann. Surg. **111**: 709, 1940.
14. Eden, K. C.: Vascular Complications of Cervical Ribs and First Thoracic Rib Abnormalities, Brit. J. Surg. **27**: 105, 1939.
15. Edwards, E. A., and Levine, H. D.: Auscultation in the Diagnosis of Compression of the Subclavian Artery, New England J. Med. **247**: 79, 1952.
16. Ehrich, F.: Zur Klinischin Symptomatologie der Halsrippen, Beitr. klin. Chir. **14**: 199, 1895.
17. Fischer: Verlauf der Art Subclav. in Einem Fall von Deutlich Entwickelter Halsrippe, Wien. med. Wchnsch. **537**, 1858.
18. Flint, E. R.: Unusual Vascular Complications of Cervical Rib, Brit. J. Surg. **24**: 622, 1937.

19. Gordon, T. E.: A Case of Cervical Rib, Brit. M. J. 1: 1395, 1901.
20. Grisson: Über Halsrippen, München. med. Wchnschr. 873, 1898.
21. Gruber, W.: Über die Halsrippen des Mensches mit Vergleichenden Anatomischen Bemerkungen, Mem. Acad. d. Sc. St. Petersbourg 7: ser. 13, No. 2, 1869.
22. Henschen, C., and Heusser, H.: So-Called Scalenus Anticus Syndrome (due to Compression of Brachial Plexus and Subclavian Artery by First Thoracic Rib), Therapy by Scaleniotomy, Chirurg. 9: 266, 1937.
23. Hodgson: Diseases of Arteries and Veins, London, 1815, p. 262.
24. Hoobler, S. W.: Syndrome of Cervical Rib With Subclavian Artery Thrombosis and Hemiplegia Due to Cerebral Embolism. Case, New England J. Med. 226: 942, 1942.
25. Imler, R. L., Jr., Hayne, R. A., and Stowell, A.: Aneurysm of the Subclavian Artery Associated With Cervical Rib. Two Cases, Am. Surgeon 17: 478, 1951.
26. Jacobsohn, H.: Das Halsrippensyndrom und Seine Chirurgische Behandlung, Arch. klin. Chir. 161: 398, 1930.
27. Keen, W.: The Symptomatology, Diagnosis and Surgical Treatment of Cervical Ribs, Am. J. M. Sc. 133: 173, 1907.
28. Kittle, C. F., and Schafer, P. W.: Gangrene of the Forearm After Subclavian Arterio-Aortostomy for Coarctation of the Aorta, Thorax 8: 319, 1953.
29. Lam, C. R.: Choice of Side for Approach in Operations for Pulmonary Stenosis, J. Thoracic Surg. 18: 661, 1949.
30. Langeron, L., and Desbonnets: Côte Cervicale avec Troubles Vasculaires Graves et Gangrène de la Main, Bull. et mém. Soc. nat. Chir. 57: 704, 1931.
31. Langeron, L., Tierny, and Paris: Côte Cervicale avec Troubles Vasculaires Graves et Gangrene de la Main, Bull. et mém. Soc. nat. de Chir. 57: 704, 1931.
32. Lenner, S.: Gangran einer operan Extremitat Ausgelost Durch ein Halsrippe, Chirurg. 10: 660, 1938.
33. Leriche, R.: Quelques Résultats Eloignés d'Opération pour Côte Cervicale. Analyse du Mécanisme Varié des Accidents Vasculaires Causés par les Côtes Cervicales, Bull. et mém. Soc. nat. Chir. 61: 1292, 1935.
34. LeVay, D. A.: Costoclavicular Compression of Brachial Plexus and Subclavian Vessels, Lancet 2: 164, 1945.
35. Lewis, T.: Vascular Disorders of the Limb, ed. 2, London, 1946, The Macmillan Company, p. 86.
36. Lindskog, G. E., and Howes, E. L.: Cervical Rib Associated With Aneurysm of the Subclavian Artery, Arch. Surg. 34: 310, 1937.
37. Lord, J. W., Jr.: Diagnostic and Surgical Aspects of the Shoulder Girdle Syndromes, New York J. Med. 55: 2021, 1955.
38. Luke, C. J., and Fountain, E. M.: Vasospasm and Occlusive Arterial Changes in the Fingers Due to Cervical Rib, Canad. M. A. J. 62: 379, 1950.
39. Matas, R.: A Summary of Personal Experience in the Surgery of the Subclavian Arteries, Tr. South. S. A. 39: 213, 1926.
40. Mac Fee, W. F.: Cervical Rib Causing Partial Occlusion and Aneurysm of the Subclavian Artery, Ann. Surg. 111: 349, 1940.
41. McGowan, J. M.: Role of the Clavicle in Occlusion of the Subclavian Artery, Ann. Surg. 124: 71, 1946.
42. Murphy, J. B.: The Clinical Significance of Cervical Ribs, Surg., Gynec. & Obst. 3: 514, 1906.
43. Ochsner, A., Gage, M., and DeBakey, M.: Scalenus Anticus (Naffziger) Syndrome, Am. J. Surg. 28: 669, 1935.
44. Oljenick, I.: Bilateral Cervical Rib—Clinical and Experimental Observations on a Case, Arch. Surg. 18: 1984, 1929.
45. Otto, K.: Ein Fall Halsrippe mit Fingergangran, Med. klin. 2: 82, 1924.
46. Patterson, R. H.: Cervical Rib and the Scalenus Muscle Syndrome, Ann. Surg. 111: 531, 1940.
47. Petronio, R.: Su un Caso di Thrombosi della Subclavia in Soggetto Con Costa Cervicale, Ospedale Maggiore (Milano) 40: 488, 1952.
48. Picot, G.: Côte Cervicale Bilatérale. Phénomènes D'Artérite du Côté droit, Mém. Acad. chir. (Paris) 61: 1430, 1935.
49. Russel, C. K.: Supernumerary Cervical Ribs and Their Effects on the Brachial Plexus and Subclavian Artery, Med. Rec. 71: 253, 1907.
50. Sénèque, J., and Lelong, M.: Côte Cervicale Bilatérale. Syndrome de Raynaud Unilatéral; Résultat Eloigné d'une Intervention Chirurgicale: Ablation de la Côte et Sympathectomy Sous-Clavière. Artériectomie Secondaire de l'Artére Humérale, Mém. Acad. de chir. (Paris 61: 1083, 1935.
51. Silbert, S.: Complete Recovery From Serious Vascular Impairment Following Removal of Cervical Rib, SURGERY 7: 392, 1940.
52. Smith, B. C.: Thrombosis of Third Portion of Subclavian Artery Associated With Scalenus Anticus Syndrome, Ann. Surg. 111: 546, 1940.

53. Streissler, E.: Die Halsrippen, Ergebn. d. Chir. u. Orthop. 5: 280, 1913.
54. Symonds, C. P.: Two Cases of Thrombosis of Subclavian Artery With Contralateral Hemiplegia of Sudden Onset, Probably Embolic, Brain 50: 259, 1927.
55. Telford, E. D., and Stopford, J. S. B.: The Vascular Complications of Cervical Rib, Brit. J. Surg. 18: 557, 1937.
56. Walshe, F. M. R., and Jackson, H., and Wyburn, M. R.: On Some Pressure Effects Associated With Cervical and With Rudimentary and "Normal" First Ribs, and the Factors Entering Into Their Causation, Brain 67: 141, 1944.
57. Webb, W. R., and Burford, T. H.: Gangrene of the Arm Following Use of the Subclavian Artery in Pulmonosystemic (Blalock) Anastomosis, J. Thoracic Surg. 23: 199, 1952.
58. Wertheimer, P.: Côte Cervicale avec Anévrysme Artériel, Mém. Acad. de chir. 61: 1373, 1935.
59. White, J. C., Poppel, M. H., and Adams, R.: Congenital Malformations of the First Thoracic Rib, Surg., Gynec. & Obst. 81: 643, 1945.
60. Willet: Reported by Smith in St. Bartholomew Hospital Records 24: 290, 1888.
61. Wilson, S. A. K., and Bruce, A. N.: Neurology, Vol. 2, ed. 2, Baltimore, 1955, Williams & Wilkins Company, p. 1210.

## ADDENDUM

Since this report, one of us (C. J. S.) has operated upon another patient for subclavian artery thrombosis associated with cervical rib disease. K. L. (M.H. 77317), a 34-year-old, right-handed woman, presented with ischemic pain in the right hand associated with pallor and weakness. There were no pulsations beyond the subclavian artery. Scalenotomy and partial cervical costectomy had been performed previously. At operation on Dec. 15, 1955, an area of subclavial arterial thrombosis was encountered that extended from the site of the thoracoabdominal axis to the beginning of the brachial artery. The operation consisted of partial claviculectomy, completion of the cervical costectomy, and insertion of a homologous by-pass arterial graft from the first part of the subclavian artery to the brachial artery. Function in the extremity has improved, but there are no palpable peripheral pulsations.

# Editorials

## Palliative Therapy in Cancer

In every case of malignant disease the desideratum is the complete eradication of the neoplasm. Unfortunately, in spite of the fact that many cancers are curable by adequate surgical removal or destruction by irradiation, there are many cases in which a cure cannot be obtained. This is usually due to delay in the institution of therapy. In such instances it is imperative that the patient, or at least responsible relatives, be informed that the lesion is not curable. It is certainly the human reaction when confronted with such a pessimistic outlook that the patient, his family, or both will grasp at straws which usually results in his consulting a quack who promises to cure the neoplastic lesion, generally for an exorbitant fee. This usually causes complete depletion of the family funds. Such reaction is not limited to the uninformed and the uneducated. Several years ago a very good surgeon, interested in oncology, who had previously investigated a well-known "cancer cure" and had found it to be a fraud, developed an incurable malignant disease. After all therapeutic methods had failed, he said, "Although I know the ———— 'cancer cure' is no good, I'm almost tempted to try it." It is, therefore, an obligation of the profession to advise patients with incurable malignant lesions about their subsequent care, and therapeutic measures which, although not curative, should be recommended and used.

Fortunately, there are now available a number of chemotherapeutic agents which are definitely tumorcidal and which can be used in humans. Nitrogen mustard and similar compounds are such agents. That they are definitely destructive to cancer cells has been proved without any question of a doubt but they are employed much less frequently than they should be. Many physicians are of the opinion that they are of principal value in lymphomas and of little value in the treatment of epithelial malignant lesions. The latter is a fallacious concept. A factor which is possibly responsible for the concept that methyl-bis is of little value in the treatment of epithelial neoplasia is that it is used half-heartedly, and generally only one course of treatment is employed. Although nitrogen mustard is tumorcidal, it does not destroy all the malignant cells and those which remain continue to grow and reproduce. For this reason, it is necessary that the administration be repeated at regular intervals, the length of time between treatments usually can be increased if the patient improves. There is considerable variation in the susceptibility of different neoplasia to methyl-bis therapy, but it has been our experience that 95 per cent of patients receiving it are benefited if the treatments are repeated.

The investigation reported by Cruz, McDonald, and Cole in this issue of SURGERY is further evidence of the value of nitrogen mustard as a tumorcidal agent. It is logical, as contended by Cole and his associates, that malignant cells which are in the blood stream or localized in a viscus as an embolus should be more vulnerable to the tumorcidal action of methyl-bis than the tumor which has begun to grow actively. It is probable that the use of nitrogen mustard prophylactically, as suggested in this investigation, may definitely decrease the incidence of distant metastases and any modality which will accomplish this will be welcomed by the profession.

*—Alton Ochsner*

## Our Medical Literature Problem

Each year this JOURNAL and several thousand others in the field of the medical sciences, are, in the aggregate, putting some hundreds of thousands of papers embodying millions of pages of print into the literature. In the whole field of the natural sciences in 1950 it is estimated that 50,000 journals published one million papers. In physiology alone it has been calculated by Rothschuh that the output of 192,000 pages in the year 1940 would require more than two years to read at two minutes per page. If estimates as to increase in publication volume are correct this figure would be more than doubled today.

The problem of locating existing information is becoming a major one in scientific research and in its application. Fifty or even thirty years ago it was possible to advise a new recruit to medical science simply "to read the literature." Today advice has to be quite different. One must say rather, "read only that part of the literature of your field which is most relevant to your specific problem." And, unfortunately, one has no valid advice to give as to how to find the most relevant literature with any assurance that much will not be missed.

The first duty of an author of a paper for a journal of primary publication is to write a concise report which presents his new findings in proper context with earlier reports in the literature. But his duty does not end there. He also has a responsibility to see to it that the report is available for indexing, abstracting, and review. Likewise, a journal of primary publication has responsibilities of the same sort because there is no point in publishing original papers unless scholars can make use of them. And the degree of usefulness of a journal varies in proportion to the completeness of indexing and abstracting of the material in it in the secondary reference journals. Some journals of primary publication now require authors to provide abstracts suitable for use in abstracting journals along with papers submitted for editorial consideration. The abstract as well as the paper itself is submitted to editorial scrutiny. Some journals print the abstracts in lieu of summary paragraphs in the paper proper. Such edited author abstracts are useful to readers when published at the head of the paper because, if they are done properly, they allow one to know whether the paper itself must be read. Editorial reviewers also find author abstracts useful in getting a thumbnail sketch of what is in a paper before

reading it, and they can evaluate an author's statements more adequately with that orientation. I refer to a somewhat more complete abstract than now appears before papers in the Journal of the American Medical Association.

The edited author abstracts so prepared can then be turned over by the journal editor to the abstracting journal, such as Biological Abstracts, and thus save the labor of an abstracter for the paper. The abstract is apt to be more accurate and complete if the author writes it because he is presumably more fully acquainted with the whole subject than an abstracter is likely to be.

An additional step has not yet been taken but would be desirable. The author might indicate the major headings under which his paper should properly be indexed in order to make it available to scholars searching indices.

I should like to propose that SURGERY adopt the policy of publishing short abstracts, usually not more than 5 per cent of the length of the paper, and that summaries and conclusions be eliminated from the body of the paper. Such abstracts should be informative rather than simply indicative of contents. They should say very briefly what methods were used, including the materials employed in the study, and they should give the significant results and conclusions. There is an art to writing abstracts and some authors may have difficulty in compressing such information into the space allotted, but other journals have found the limit adequate.

If this system were universally adopted by medical journal editors a large step would have been taken toward making medical science literature more available to research workers. The time is past when scholars can search every journal for data on subjects of their interest. Such activity is so time-consuming today that no one can successfully pretend that he does it. It is becoming obligatory upon each journal to contribute to the job of indexing and abstracting the material that it publishes, which means getting its authors to assist in the job. More progress has been made by nonmedical than by medical science journals. I should like to see SURGERY lead in this move to improve the usefulness of its publication and help in clearing up the bibliographic pandemonium in which we find ourselves today.

—*Maurice B. Visscher*

# Appraisal of Progress in Surgical Therapy

CONDUCTED BY WARREN H. COLE, M.D.
ASSISTED BY
J. GARROTT ALLEN, M.D. CLARENCE DENNIS, M.D.

## A CONSIDERATION OF CERTAIN BENIGN LESIONS OF THE ESOPHAGUS

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TWO benign lesions which currently occupy the minds of those who are interested in the diseases of the esophagus are peptic ulcer with esophagitis and achalasia. Though they have nothing in common, either as regards their etiology or their clinical manifestations, the problems presented by the efforts of the surgeon to relieve them present certain similarities which justify the inclusion of a discussion of each of these conditions from the point of view largely of personal experience as herein set forth.

### PEPTIC ULCER AND ESOPHAGITIS

Although in recent years there has been an intense interest in the subject, the fact remains that relatively little is actually known about the etiology of esophagitis. That an acute, subacute, or even chronic inflammatory process may involve the esophagus at any level is well known, but it is also apparent that, in the majority of instances, the disease is confined to the lowermost portion. The reason for this localization is not clearly understood. If regurgitation of acid and peptic secretions from the stomach into the esophagus is the usual cause of esophagitis, as contended by many authors, the explanation becomes obvious, because it may be assumed that the effect of the gastric juices might not be observed at higher levels. Variation in mucous membrane susceptibility, however, may also be a factor. It is possible that the mucosa of the middle and, particularly, the upper portions of the esophagus is much more resistant to the effects of irritating substances which bathe its surface. That such may be the case is suggested by the observation that postoperative esophagitis just above an esophagogastric anastomosis, following resection of the distal portion of the esophagus with preservation, in each instance, of the major portion of the stomach, is less likely to develop when a long segment has been removed than after limited resections of the lower end. It has been suggested that the reason for this phenomenon might be that the neutralizing effect of saliva is more active in the upper levels of the esophagus than in the lower.

Received for publication March 19, 1956.

The importance of the effect of regurgitation of gastric secretions into the lower esophagus as the chief etiological agent in the production of esophagitis is not clearly defined. There is little doubt that this phenomenon may be a factor in many instances, but it would seem that it is effective only under certain special conditions. There appear to be two reasons why this mechanism is so widely accepted as the cause. The first has to do with the large amount of experimental work which has been done on animals, almost exclusively on dogs. The importance of many of the observations made in this way is obvious insofar as they concern the canine species, but their significance when applied to the problem as it is encountered in human beings is not entirely clear. The second reason rests upon the almost universal assumption made by clinicians that when a patient experiences pyrosis (commonly referred to as "heartburn"), he must be suffering from esophagitis. This symptom, however, is common in the complete absence of esophagitis. It may actually result from any of a variety of stimuli. It may arise merely from stretching the esophagus, as shown by Jones and Chapman[3] with balloon distension studies. Actually the majority of complaints of pyrosis are not due to esophagitis. This is true, likewise of substernal distress or pain which may be caused by a variety of conditions. In fact, a diagnosis of esophagitis, though suggested by these symptoms and often likewise by certain appearances observed by roentgen examination, cannot be conclusively established without esophagoscopic examination and then often only by removal of tissue for microscopic examination.

Another observation of importance in the discussion of the possible role of regurgitation of gastric secretions as an etiological factor is that true esophagitis is rarely found among patients who have hiatus hernia of the frequently observed sliding type. There can be little doubt that patients with this condition experience repeated regurgitation of gastric juices into the lower esophagus, yet in an experience of over 400 such cases, esophagitis was encountered in only 3 instances. Furthermore, regurgitation of barium into the esophagus can be demonstrated in practically every person examined by fluoroscopy no matter whether a hiatus hernia is present or not, and yet these individuals do not have, nor do they necessarily ever develop, esophagitis. It appears, therefore, that conditions other than the effect of regurgitated gastric secretions alone must exist if esophagitis is to occur.

It is generally accepted that duodenal ulcers occur among persons who have an individual susceptibility. There is apparently an "ulcer diathesis" which seems to predispose those who have it to the development of that disease. However, so far as I am aware, the actual etiology of duodenal ulcer is still unknown. It should be pointed out emphatically that esophagitis with ulceration likewise tends to develop in persons with a peculiar susceptibility. In fact, in this group of patients the coincident occurrence of duodenal ulcer is strikingly high (38 per cent in a series reported recently[5]). Furthermore, a history of the occurrence of a duodenal ulcer in the past or the finding of a deformity of the duodenum on roentgen examination of patients with esophageal ulcers and inflammation is an even more frequent occurrence. Patients with so-called "peptic esophagitis" and ulcer, therefore, are usually those who have an ulcer-forming tendency.

As actually observed, peptic esophagitis and ulceration is found most frequently in the presence of a distinctly abnormal anatomic arrangement of the esophagus, cardia, and upper stomach. This condition is characterized by a definite shortness of the esophagus. The esophagogastric junction (cardia) often lies several inches above the diaphragm, and the first portion of the stomach comprises a tubular segment lying in the lower mediastinum. To the uneducated eye this arrangement may not be obvious by roentgen examination although it can almost always be identified. When exposed at the operating table, however, the condition is readily recognized and it is often astonishing to observe how high in the mediastinum the gastroesophageal junction may be. It is only at the operating table, on the other hand, that it can be shown that, in the majority of instances, this thoracically located tubular segment of stomach is not attended by the presence of a pouch of peritoneum which could be called a hernia sac. Furthermore, there is no possibility whatever in these patients with a short esophagus and thoracic stomach of altering the anatomic location of the viscera in the direction of placing the cardia below the diaphragm as in the ordinary repair of a hernia of the sliding variety. It should be recognized that this condition, with its absence of a true hernia sac and its strikingly characteristic anatomic pattern, is not actually a hernia but rather a structural abnormality which is probably developmental in origin.

It has been contended that the high-lying position of the cardia in patients with esophagitis and stricture is caused by shortening resulting from cicatricial contracture. It is difficult to believe, however, that this mechanism could ever be responsible for the displacement of the gastric cardia from its normal position one or more inches below the diaphragm to a new location in the chest several inches above the diaphragm. Furthermore, it is unlikely that this or any other mechanism on an acquired basis could explain the striking abnormality of the configuration of the proximal portion of the stomach which cannot be altered even when an effort is made to change the shape of the resected specimen.

It is plausible to assume that this condition is usually congenital in origin. Confirmation of this assumption is suggested by the fact that a short esophagus and thoracic segment of stomach with a stricture at the cardia, where it lies in the chest above the diaphragm, may actually be observed in very young infants. Fig. 1 shows the typical findings of short esophagus, thoracic stomach, and stricture in an infant less than 2 months of age.

The fact remains that, no matter what the explanation of its occurrence may be, patients with a short esophagus and thoracic segment of stomach are particularly prone to the development of ulceration and inflammatory stricture. The question then arises as to whether the ulcerations (presumably "peptic") develop in the high-lying lower esophagus or in the thoracically located tubular segment of stomach. More often than not they actually occur at the esophagogastric junction (or cardia), so that one could hardly determine whether they arose primarily in gastric or esophageal mucous membrane. That ulcers may develop in areas of esophagitis just above the cardia is certainly true, but in many instances the inflammatory process and ulceration arises chiefly within

the tubular segment of the stomach as it lies in the chest. This fact is not always recognized by the surgeon who, if he performs a limited resection, may unwittingly leave a segment of stomach behind by transecting the tubular segment below the cardia. An example of this occurrence is illustrated in Figs. 2 and 3. Fig. 2 shows diagrammatically the anatomic arrangement of the upper

Fig. 1.—Roentgenogram of the esophagus of an infant less than 2 months of age who had a congenitally short esophagus, thoracic segment of stomach, and a stricture of the lower esophagus at the cardia.

stomach, cardia, and lower esophagus in a patient 60 years of age who was suffering from peptic ulceration and stricture formation presumably of the esophagus. The lesion, however, was actually located in the lower portion of a long tubular segment of stomach which was mistaken for esophagus at roentgen examination. At operation, performed before the importance of carrying out a more extensive resection was recognized, the proximal level of transection was,

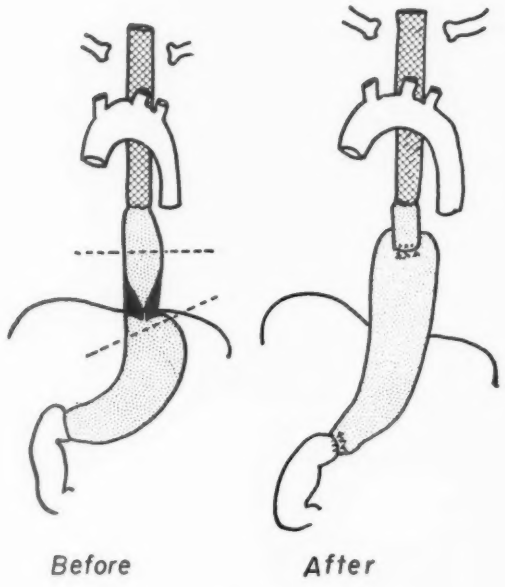


Fig. 2.

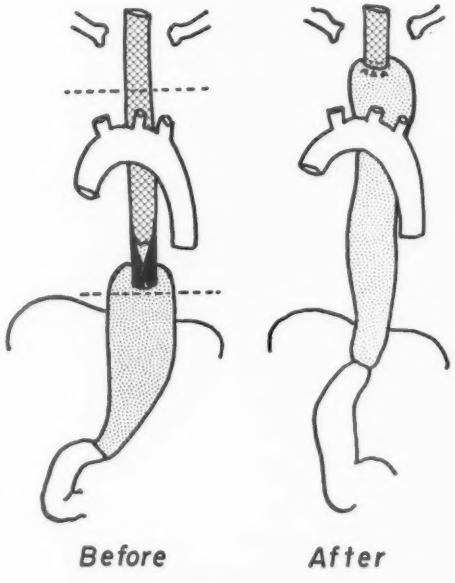


Fig. 3.

Fig. 2.—Patient B. J. (first operation). Diagram showing, at the left, the location of stricture in the thoracic segment of stomach several inches below the cardia. The dotted lines delimit the portion which was resected. At the right, the relation of the organs after resection is shown. Note (1) that a short section of the thoracic stomach was retained because of failure to recognize the true nature of the condition, and (2) that a pyloroplasty was performed because of a stenosis resulting from previous duodenal ulcerations.

Fig. 3.—Patient B. J. (second operation). Diagram showing, at the left, the location of the recurrent stricture in the thoracic gastric segment preserved after the limited resection performed five years previously. The dotted lines show the extent of the second and more extensive resection. At the right is illustrated the location of the new anastomosis high in the mediastinum. Note the position of the stomach to the right of the aortic arch. (A left thoracotomy incision was employed for each procedure.)

in fact, just below the cardia so that a short segment of stomach remained below the esophagogastric junction, which was not diseased. An anastomosis was performed in the lower mediastinum using this short residual portion of thoracic stomach as the upper edge. Five years later the patient returned with a recurrent ulcer and stricture, requiring this time a resection which was carried across the esophagus at a level well above the aortic arch. It was only after the resected specimen was examined that the true nature of the condition became apparent and it was in fact recognized that a small gastric segment had been left attached to the esophagus at the first resection. Fig. 3 shows the condition before the second operation and the extent of the resection performed at that time. Cases such as this remind one of the contention of Barrett[1] and others that ulcers and strictures of the esophagus practically always develop in gastric mucosa. Certainly they are usually at or very near the cardia, and the contention that, when seen above this level, they always occur in aberrant islands or upward extensions of gastric mucous membrane would seem to be of very little practical importance.

The concern of the surgeon is rather with the indications for operation and the nature and extent of the procedure which should be employed. The indications for operation can be clearly defined. In general they are precisely the same as those for operating upon an ulcer of the duodenum. They are as follows: (1) Hemorrhage from erosion of a blood vessel large enough to cause continuous bleeding; (2) penetration or perforation; (3) intractable pain not relieved by a proper medical regimen, and (4) obstruction from cicatricial contracture not successfully relieved by dilatation. There is never any doubt about the necessity for operating in the presence of bleeding. Perforation is of rare occurrence and not often recognized early enough to permit a direct attack upon the lesion itself. Intractable pain even in the absence of complications of the ulcer, is a more frequent indication, merely to provide the relief the patient so eagerly seeks. The most frequent indication for surgery, however, is the presence of a stricture which cannot be handled successfully by bougienage.

Because a clear understanding is so important from the point of view of treatment, the term "stricture" should be defined. One should differentiate between the terms "stenosis" and "stricture." So far as the effects of esophagitis are concerned, a stenosis exists usually as a result of swelling from inflammatory edema but without ulceration and destruction of the mucosa. This condition is reversible and, with the subsidence of the swelling, an adequate lumen is restored. Definite benefit often results from gentle dilatation with appropriate instruments when the process is in this phase of its development, and surgery is not required. In the presence of an ulcer, however, the situation is entirely different. Here, especially when the ulceration is extensive or oft repeated, and particularly when the destruction of mucous membrane is circumferential in extent, the end result of healing is the cicatricial contraction of scar tissue. This condition, unlike the former, is not reversible and instrumental dilatation cannot be expected to produce lasting benefit. Temporary relief may be experienced as a result of tearing and disruption of the scar tissue,

but as healing takes place the stricture only recurs and makes further treatment necessary. The dangers of perforation, the impossibility of obtaining lasting relief, and often the wish to avoid further discomforts on the part of the patient demand the employment of surgical means to overcome the difficulty in cases such as this.

The choice of operation, however, is not always as easy to make as the decision to intervene. The surgical objectives must be kept in mind. Two purposes are chiefly important. The first is to eradicate the bleeding or painful ulcer or the obstructing stricture. This can sometimes be accomplished by a relatively simple procedure such as an esophagoplasty, as in the case of a stricture of very limited longitudinal extent, or a local resection in any case. It should be mentioned, however, that, as in duodenal ulcer, local excisions and resections of limited extent are sometimes attended by failures resulting from the development of new ulcers and areas of esophagitis at or just above the suture line. Because we are dealing here with a disease having as its basis certain physiologic alterations in common with duodenal ulcer and with patients who, therefore, are doubtless more prone to develop ulcerations of the type for which the operation is being performed, it is important to give consideration to the development of a procedure which, like the so-called subtotal gastrectomy for duodenal ulcer, may be depended upon to assist in the prevention of recurrences of the disease. This may be accomplished in two different ways.

In the first place, one may take advantage of the observation that esophagitis rarely develops in the upper portion of the organ by resecting a long segment of esophagus and only as much stomach as is permitted to make it possible to perform a high esophagogastric anastomosis. To be most effective the level of division of the esophagus should be above the arch of the aorta (Fig. 3). In order to perform an anastomosis at this level, of course, it is necessary to preserve almost the entire stomach. This technique has been advocated by other surgeons and, for the most part in my experience, has been remarkably satisfactory. However, in a series of 33 patients treated in this manner, there were 2 who developed anastomotic strictures two or more years later requiring treatment by bougienage.[5] It should be mentioned that anastomosis was not always above the aortic arch in all of these cases so that theoretically at least the level of transection of the esophagus may not always have been high enough.

A second approach to the problem is based upon the assumption that in these peculiarly susceptible people a recurrence of the difficulty might be prevented by reducing the chances of regurgitation of acid and pepsin from the stomach. This can be accomplished, to a large extent at least, by performing an extensive resection of the proximal portion of the stomach along with as much of the lower esophagus as is consistent with a complete excision of the diseased segment. As shown in Fig. 4, this has been done in a manner to remove all of the fundus, a large part of the body, and the majority of the lesser curvature. A tube of stomach along the greater curvature is made by partial closure of the remaining portion and the anastomosis is made end-to-end with the esophagus. The secretion of acid is, of course, not entirely eliminated in these

patients because the majority of the antrum is retained. Dragstedt's valuable work on gastric physiology in relation to the formation of ulcerations of the stomach suggests that unless there is delay in the emptying of the stomach, this danger is probably slight. An important part of the operation, therefore, is to make provision by pyloroplasty, or gastrojejunostomy if preferred, for the relief of any degree of pyloric or duodenal stenosis, no matter how slight, which

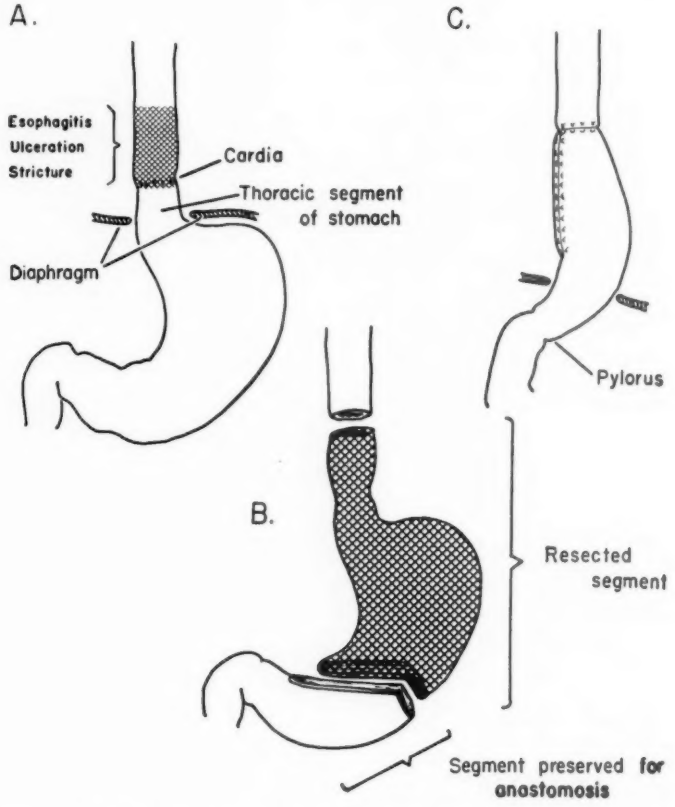


Fig. 4.—Diagram illustrating (*A*) the usual location of the lesion, (*B*) the relative amounts of stomach and esophagus resected in the extensive partial gastrectomy and esophagectomy employed in certain instances with the intention of reducing the production of acid and pepsin by the remaining stomach, (*C*) the anastomosis and gastric closure.

might be present as a complicating factor in these cases. In fact, this principle of insuring prompt emptying of the stomach is of supreme importance in every case of proximal partial gastrectomy, esophagectomy, or esophagoplasty no matter what the underlying disorder may have been. If this important detail is not taken care of symptoms may develop from the backing up of gastric contents into the stomach or gastric ulcers may occur. I have known of two fatalities from perforation of acute gastric ulcers which had developed under these circumstances after esophagectomy for carcinoma.

So far as the end results following extensive proximal resection of the stomach in peptic ulcer of the esophagus and cardia are concerned, it is too early to

determine and too few cases have been done. However, those patients who have been treated in this manner have thus far remained free from recurrent ulcer or esophagitis for periods of from a few months to several years.

Space does not permit a discussion of other methods calculated to prevent recurrent esophagitis, such as the interposition of a segment of jejunum or even the complete bypassing of the stomach itself. Esophagitis has been known to occur after the latter procedure and even after total gastrectomy with esophagojejunal anastomosis. Furthermore, recent experimental work by Merendino and Dillard[4] on dogs introduces another factor, namely pyloroplasty, which of itself would doubtless protect the esophagus against esophagitis after proximal gastrectomy and esophagectomy, so that on the basis of these experiments at least conclusions cannot be made on the value of jejunal interposition alone even in the dog.

In conclusion it can be said that carefully planned surgical resections should be resorted to whenever a good indication for operation exists. A recent report[5] indicates that "if a careful choice of operative procedure is made to suit the conditions encountered . . . a satisfactory clinical result can be anticipated in at least 90 per cent of the patients."

## ACHALASIA

The other benign disorder of the esophagus about which there is considerable discussion at the present time is the peculiar condition commonly called cardiospasm. The choice of the term, "cardiospasm" to designate this disease is unfortunate because, in the first place, the condition is a disease of the esophagus itself without involvement of the cardia, and because, although an element of esophagospasm often exists, spasm in itself is not the outstanding alteration. On the other hand, no other term is entirely satisfactory. The designation "achalasia" proposed by Hurst and Rake[2] in an effort to suggest the mechanism at work in the production of the disease is preferred by some. The descriptive word, "mega-esophagus," is as good as any, and if emphasis on our lack of knowledge of the etiology of the disease is desired, the term "idiopathic dilatation" may be employed.

The etiology is unknown, but from the standpoint of understanding the clinical aspects of the disease and particularly the choice of surgical treatment in those few cases where conservative measures fail, it is important to realize that two types of this disorder can be differentiated. In a recent publication these were described in detail.[6] The differentiation can be made on the basis of the clinical history, roentgen examination, and anatomic appearance as disclosed at operation. In the first and larger group of patients, the esophagus is of enormous size, often tortuous in contour, completely lacking in peristaltic activity even after long periods of observation under the fluoroscope, and at operation presents a thin-walled, narrow, atrophic-appearing distal segment. The only symptom is that of the dysphagia so clearly recognized clinically. The second and smaller group comprises those where the dysphagia may be just as intense, but where at some time during the history of its development, the condition has been attended by attacks of esophageal pain, doubtless resulting from

spasm. This may have occurred only early in the disease. At roentgen examination irregular peristaltic activity, often of a reverse type, is observed and the esophagus is never as large in diameter as in the first group. Finally, at operation, although the esophagus is moderately dilated and hypertrophied above and the lower segment narrowed in relation to it, the difference is not as striking as in the first group. Furthermore, the lower segment, although somewhat narrow, is characterized by a striking degree of hypertrophy of the circular muscle fibers.

Patients with each of these two types have been observed for periods of many years without obvious change and there is no evidence to suggest that one type represents a phase of the development of the other.

Both types seem to respond equally well to treatment by dilatation and the degree and permanence of the benefit thereby obtained is often remarkable. In this respect the disease is obviously entirely different from esophagitis with stricture formation. In no case of mega-esophagus is there ever any evidence of scar tissue unless produced instrumentally, and this is a rare occurrence.

While treatment by bougienage is usually successful, and while there is general agreement that it should be employed whenever possible, there are cases where surgery may be required. These comprise the small group in which the relief obtained by dilatation is insufficient in degree or too short in duration to make it practicable, and the smaller number of patients who refuse to have treatment carried out by this means. An occasional patient may find it impossible to travel conveniently to obtain the treatments at a distance, and there are those who cannot learn to use a mercury bougie on themselves.

A large variety of surgical procedures has been tried in the past including esophagoplasty, esophagomyotomy, side-tracking esophagogastric anastomosis, and esophagectomy with or without a limited or extensive partial gastrectomy. It appears from the recent literature and from personal experience that of any of the procedures outlined esophagomyotomy is least likely to be attended by unpleasant after-effects and complications. Actually this procedure is preeminently satisfactory in that group of cases where a band of hypertrophied circular muscle fibers is found at the lower end of the esophagus (Type 2). In this group no complications have arisen,[6] and with the exception of one patient who still has rare transient attacks of pain, the results have thus far been completely satisfactory.

On the other hand, although in the group with a thin-walled, atrophic lower segment the narrowing can be overcome completely by longitudinal incision and circumferential closure,[7] a small number of patients have experienced after-symptoms and complications as reported in the article mentioned above.[6] Lateral anastomosis between the stomach and esophagus, although not employed in my experience, has been attended by a high incidence of esophagitis in the hands of others. Personal experience with esophagoplasty has led to some interesting observations which may have an important bearing on the problem. In common with other surgeons I have observed a few patients who have experienced massive hemorrhages or anemia from chronic blood loss following the performance of esophagoplasty for achalasia of the narrow lower segment group. Although

the assumption is usually made that this is due to esophagitis and that the esophagitis is due to acid-peptic regurgitation from the stomach, it was found in the careful study of the cases mentioned[6] that acute gastritis was the source of the bleeding in 6 of the 8 patients whose blood loss was shown definitely to be from the upper gastrointestinal tract. In the other two patients gastritis was suspected but not actually proved.

Gradually it became apparent that an appreciable number of the patients with mega-esophagus have a functional disturbance of the pylorus and antrum of the stomach which produces often a striking degree of delay in the emptying of the stomach. This fact was recognized before its importance was appreciated as a result of the recent work of Dragstedt on the mechanism of antral stimulation of acid secretion. Thus the occurrence of gastritis in the group of patients already referred to was undoubtedly associated with this pyloric delay. In several patients relief has been obtained by performing a pyloroplasty. In the two patients who bled severely an extensive proximal partial gastrectomy was performed with complete relief. Wangensteen's[8] earlier advocacy of extensive proximal partial gastrectomy with resection of the lower esophageal segment is of significance in view of these experiences.

The importance of delayed gastric emptying from pylorospasm or any other cause is of further significance when it comes to the evaluation of the degree of relief from dysphagia produced by any operation upon the lower esophagus for achalasia. If after such an operation there remains any cause, whether functional or mechanical, for delay in the passage of gastric contents through the pylorus, the patient may be led to believe that the operation upon his esophagus has been unsuccessful. In several such cases at fluoroscopic examination, passage of the ingested barium meal into the stomach was prompt, but as the stomach became full and remained so for several hours, the patient felt as though he still had his former difficulty.

Primary resection as a method of treatment for mega-esophagus, though advocated by some, is probably unnecessarily radical. If it is chosen, however, with the intention of reducing the incidence of postoperative esophagitis and gastritis, it should be extensive, as mentioned before.

In summary, so far as the surgical treatment of achalasia is concerned, there is little doubt that in properly selected cases esophagomyotomy can be relied on to produce complete and lasting relief from dysphagia with a minimum of complications and sequela. On the other hand, if for any reason an esophagoplasty or even a resection appears to be the operation of choice, the surgeon should keep in mind the possibility of dysfunction of the pylorus and take measures to overcome this occurrence whenever it is found.

These two benign conditions of the esophagus, "peptic" esophagitis with ulcer formation and achalasia, will provide, for some time to come, ample material for discussion and disagreement both as to the nature of the disease and the rationale of surgical treatment. Experience with surgery in the treatment of these disorders has, however, already improved our understanding of them to a considerable extent, and luckily has been attended by a sufficiently satisfactory degree of success to justify our continued efforts.

REFERENCES

1. Barrett, N. R.: Chronic Ulcer of the Esophagus and Esophagitis, Brit. J. Surg. 38: 175, 1950.
2. Hurst, A. F., and Rake, G. W.: Achalasia of the Cardia (So-Called Cardiospasm), Quart. J. Med. 23: 491, 1930.
3. Jones, C. M., and Chapman, W. P.: Studies on the Mechanism of Pain of Angina Pectoris With Particular Relation to Hiatus Hernia, Tr. A. Am. Physicians 57: 139, 1942.
4. Merendino, K. A., and Dillard D. H.: The Concept of Sphincter Substitution by an Interposed Jejunal Segment for Anatomic and Physiologic Abnormalities at the Esophagogastric Junction (With Special Reference to Reflux Esophagitis, Cardiospasm, and Esophageal Varices), Ann. Surg. 142: 486-509, 1955.
5. Sweet, R. H., Robbins, L. L., Gephart, T., and Wilkins, E. W., Jr.: The Surgical Treatment of Peptic Ulceration and Stricture of the Lower Esophagus, Ann. Surg. 139: 258-268, 1954.
6. Sweet, R. H.: Surgical Treatment of Achalasia of the Esophagus, New England J. Med. 254: 87-95, 1956.
7. Sweet, R. H.: Idiopathic Dilatation of the Esophagus, S. Clin. North America 27: 1128, 1947.
8. Wangensteen, O. H.: A Physiologic Operation for Mega-Esophagus: (Dystonia, Cardiospasm, Achalasia), Ann. Surg. 134: 301-318, 1951.

## Calendar of Surgical Meetings

### 1956

THE AMERICAN ACADEMY OF NEUROLOGICAL SURGERY. *Annual Meeting,* Nov. 1-3, 1956, Camel Back Inn, Phoenix, Ariz. Secretary, Eben Alexander, Jr., M.D., Bowman Gray School of Medicine, Winston-Salem, N. C.

AMERICAN ASSOCIATION FOR THE SURGERY OF TRAUMA. *Annual Meeting,* Oct. 4-6, 1956, The Biltmore, Santa Barbara, Calif. Secretary, James K. Stack, M.D., 700 N. Michigan Ave., Chicago 11, Ill.

AMERICAN COLLEGE OF SURGEONS. *Clinical Congress,* Oct. 8-12, Civic Auditorium, San Francisco, Calif. Secretary of the College, Michael L. Mason, M.D., 154 E. Erie St., Chicago 11, Ill.

AMERICAN MEDICAL ASSOCIATION. *Clinical Session,* Nov. 27-30, 1956, Civic Auditorium, Seattle, Wash. Secretary, Council on Scientific Assembly, A. M. A., 535 N. Dearborn St., Chicago 10, Ill.

LATIN AMERICAN CHAPTER OF INTERNATIONAL SOCIETY OF ANGIOLOGY. *Third Meeting,* Nov. 8-11, 1956, Havana, Cuba. President, Armando Núñez Núñez, Calle 25 No. 510, Vedado, Havana, Cuba.

NEW ENGLAND SURGICAL SOCIETY. *Annual Meeting,* Oct. 5 and 6, 1956, Poland Springs House, Poland Springs, Maine. Secretary, Richard Warren, M.D., Peter Bent Brigham Hospital, 721 Huntington Avenue, Boston 15, Mass.

SOUTHERN SURGICAL ASSOCIATION. *Annual Meeting,* Dec. 4-6, 1956, the Boca Raton Club and Hotel, Boca Raton, Fla. Deadline for papers, Sept. 20, 1956. Secretary, George G. Finney, M.D., 2947 St. Paul St., Baltimore, Md.

### 1957

AMERICAN UROLOGICAL ASSOCIATION. *Annual Meeting,* May 6-9, 1957, William Penn Hotel, Pittsburgh, Pa. Deadline for papers, Jan. 1, 1957. Secretary, Samuel L. Raines, M.D., 188 S. Bellevue Blvd., Memphis, Tenn.

THE CENTRAL SURGICAL ASSOCIATION. *Annual Meeting,* Feb. 21-23, 1957, The Drake Hotel, Chicago, Ill. Deadline for papers, Oct. 15, 1956. Secretary, Charles D. Branch, M.D., 102 North St., Peoria, Ill.

THE PACIFIC COAST SURGICAL ASSOCIATION. *Annual Meeting,* Feb. 4-6, 1957, El Mirador Hotel, Palm Springs, Calif. Secretary, Carleton Mathewson, Jr., M.D., Stanford University Hospital, San Francisco 15, Calif.

PAN-PACIFIC SURGICAL ASSOCIATION. *Annual Meeting,* Nov. 14-22, 1957, Honolulu, Hawaii. Director General, F. J. Pinkerton, M.D., Room 230, Young Building, Honolulu, Hawaii.

THE SOCIETY OF UNIVERSITY SURGEONS. *Annual Meeting,* Feb. 7-9, 1957, Columbus, Ohio. Secretary, James Hardy, M.D., Hospital of the University of Mississippi, Jackson, Miss.

# In Memoriam

## John Albert Key
## 1890–1955

TO THOSE who knew of the severe cardiac disability from which he suffered following a coronary thrombosis nearly ten years ago, there was no surprise in the announcement of the death of John Albert Key on Aug. 7, 1955. While the news that his spirit had vanished into the great beyond caused sadness and a deep sense of loss to his many friends, this feeling was mingled with gratitude that he had been spared so many years in order to continue his research and orthopedic practice, and to stimulate so many of his associates and others to exert themselves in similar fields. Only those who knew him had any idea of the courage he had shown in continuing with his work in spite of constant anginal attacks, or the gallantry he displayed in going on right to the end facing the ever imminent risk of disaster. Nitroglycerine was his constant companion and one might even say that he lived by it. I think his chief stimulus during these years was the feeling that he had important work to finish and that he must get as much done as possible before he died. This activity in spite of severe handicap was typical of the man because courage and perseverance were shown throughout his life.

Albert was born in Jackson, Mississippi, April 21, 1890, the son of Dr. John Waller Key, D.D.M., and of Sara Endicott Heathman Key. He was brought up in St. Petersburg, Fla., and attended the public schools there. Indeed, he always boasted of being a Florida "cracker." His family was in modest circumstances and only his own determination and persistence in finding means to bear its expense enabled him to secure a higher education. He graduated from the Alabama Polytechnic Institute with the degree of B.S. in 1913, and then entered the Johns Hopkins Medical School, but had to discontinue his studies for a year, in order to accumulate more cash reserve. He re-entered in 1914. His was the famous class whose members completed their medical training overseas in 1918 as members of the United States Army Medical Corps. This arrangement was largely the result of the planning of Dr. John T. Finney, Professor of Surgery, who foresaw, as early as 1916, that the United States was likely to be drawn into the First World War, and began organizing a hospital unit at the Johns Hopkins Medical School and Hospital. Medical students from the junior year were enrolled in this unit with the rank of private, and given the opportunity of serving as interns so that they could continue their medical and clinical studies while on active service. Dr. Key was one of thirty-two men chosen to go overseas with the U. S. General Hospital No. 18. In June, 1917, the

Unit landed at St. Nazaire, France, and shortly after moved up to the front battle area in the vicinity of Nancy. The students worked as interns when there were patients, and at other times constituted a clean-up squad. During the winter of 1917 and 1918, Albert worked in the orthopedic ward of the Hospital. In April, 1918, those students who had served their full time with the Hospital were awarded the degree of Doctor of Medicine by Johns Hopkins University, and at the same time were commissioned as First Lieutenants in the Medical Corps of the United States Army continuing to serve with the Hospital Unit.

By the end of the war, Albert was convinced that he wanted to become an orthopedic surgeon. He went to Boston and applied for the orthopedic residency and training program which was given jointly at the Boston Children's Hospital, the Massachusetts General Hospital, and the Harvard Medical School. No appointment was immediately available but he was able to obtain a six-month appointment as surgical intern at the Children's Hospital under Dr. J. S. Stone. This filled the interim of waiting for his orthopedic residency and he also had time left to fill in with research in hematology under Dr. Frances Peabody, Professor of Medicine, and later with Dr. Walter Cannon, Professor of Physiology, in the physiology of the gastrointestinal tract. Following completion of his two years' orthopedic residency, he was appointed Resident Orthopedic Surgeon at Deveraux Mansion, a convalescent facility for patients with orthopedic problems in Marblehead which was conducted by Dr. Joe E. Goldthwaite and Dr. Robert B. Osgood. This appointment left some time free for the completion of his studies previously begun under Drs. Peabody and Cannon. Following completion of his work there, he returned to Baltimore, the city of his first love, where he entered orthopedic practice and received the appointment of Instructor in Orthopedic Surgery at the University of Maryland Medical School.

It was just about this time that those unusual men, Forrest Adair, Freeland Kendrick, and Dr. Michael Holk, leaders in the Mystic Order of the Shrine, were engaged in formulating their plans for organizing what later became known as the Shriners Hospitals for Crippled Children, scattered throughout the United States. These men decided that one of the first hospitals should be built in St. Louis, and that facilities should be established not only for treatment, but for research. This gave Dr. Robert Osgood, who was serving as a member of the Medical Advisory Board and who had already been impressed by the quality of Albert's investigative work, the opportunity to nominate him Director of Research. At the same time Dr. Leroy Abbott, then working at the University of Michigan Medical School, was appointed Chief Surgeon of this hospital. Both men assumed their positions in 1924, and in working together became the closest of friends. This friendship continued even after Dr. Abbott moved to San Francisco and it widened to include Dr. Harold Hitchcock, a friend of Dr. Abbott's. With these two com-

panions, Dr. Key spent many happy holidays on fishing trips in the Far West, and these convivial interludes continued even after he had become disabled by illness.

The move to St. Louis was the beginning of Dr. Albert Key's career as a clinical orthopedic surgeon in that city, and also as an investigator. He became associated with the Washington University, and, in 1931, was appointed Professor of Clinical Orthopaedics and head of the Division of Orthopaedic Surgery.

There were two great driving forces in the life of Albert Key: first, the love of research, which seemed to be almost a physical necessity to him, and

Edwyn Portraits

JOHN ALBERT KEY

second, his love of friends and family. Research was never made easy for him, and he had to carry on this work at great sacrifice both of time and personal funds. His devotion to research was well illustrated during a period extending over many years. During this time, he devoted his mornings to hospital and clinic work, and his afternoons to work in his research laboratory. It was only when the clock pointed to 5 P.M. that he would terminate his academic duties and go down to his office for private practice from which he derived his living.

His interests and investigations were varied, and it was as recently as 1952 that he told his friends that he had decided he had to learn more about chemistry in order to pursue biochemical research. He engaged a private

tutor and went to work studying various textbooks of biochemistry, trying to bring his old knowledge up to date in terms of the newest chemistry. His industry was enormous and his scientific contributions to current medical journals included 215 titles, mostly reports of research or clinical articles. This makes an average of six articles per year for each of his thirty-seven years of professional life. His interests were varied, and his research ranged over a wide variety of different subjects. In between times he found time to translate, from the French, Leriche and Policard's book entitled *Normal and Pathological Physiology of Bone, Its Problems,* and have it published. One of his great contributions was joint authorship with Dr. H. Earle Conwell of Birmingham, Ala., of a book entitled *The Management of Fractures, Dislocations and Sprains,* which has become a standard textbook and has been revised from time to time and kept up to date. Indeed, his last act before he died was to complete the last revision.

As a physician he was outstanding, and he was also a brilliant surgeon. He made a real contribution to the surgery of ruptured intervertebral disc for which condition he performed many operations, and of later years chiefly under local procaine anesthesia. His was the first idea of the use of a compression clamp in the arthrodesis of the knee joint, the forerunner of the whole concept of impaction of bones to promote healing. He combined both the qualities of an outstanding clinical surgeon and diagnostician with those of an imaginative investigator.

It was chiefly as a speaker that he was known to members of the medical profession. He was outspoken in criticisms, sometimes to the point of being caustic, but he always did it in his own style which was partly humorous and partly picturesque so that he rarely gave offense. He believed in speaking his mind at medical meetings when he thought the situation called for it, and his appearance on the stage would always be greeted with a laugh, but also with rapt attention. Everyone knew that what he said would honestly express what he thought. He had a homespun attitude of keeping his feet on the ground and of translating theories into well-understood principles and common sense and of mingling criticism with humor.

Albert was popular and his circle of friends constantly widened. He exerted an ever increasing influence among scientific groups. Many distinctions were bestowed upon him. Among these was the Presidency of the American Orthopaedic Association, the highest honor for an orthopedic surgeon in the United States. His Presidential Address before that body, in 1946, still stands out as one of the best in many years. It was an attack upon the rigid educational and training requirements of the Certifying Boards of the Surgical Specialties, and he analyzed the early careers of various distinguished orthopedic surgeons, and compared the flexible and varied educational programs they had followed, with the modern requirements laid down by the Board. His remarks were devastating in their effect and were followed later by modification of some of the Board requirements in the direction of greater flexibility.

For many years he served as the Representative of Orthopaedic Surgery on the Program Committee of the Surgical Forum of the American College of Surgeons. He also acted as moderator of the Orthopaedic Program of the Forum at the annual meeting of the College. He helped organize the Orthopaedic Research Society, of which he was President at the time of his death. During World War II he served as Orthopaedic Consultant to the Surgeon General of the Army, and as a member of the Orthopaedic Sub-Committee of the Surgical Section of the National Research Council.

Testimony of the high quality of his scholarship is given by his membership in Alpha Omega Alpha, and Phi Beta Kappa. He belonged to innumerable medical societies, including the American Orthopaedic Association, the American Academy of Orthopaedic Surgeons, the American Medical Association, the American Surgical Association, the American College of Surgeons, the American Radium Society, the Missouri Medical Association, the Robert Jones Orthopaedic Club, the Orthopaedic Research Society, and the Clinical Orthopaedic Society to mention only a few.

His family life was close and cherished. He met his wife, Eleanor Laurenson Meyer, when he was serving overseas in World War I. She was a nurse attached to the Johns Hopkins Unit No. 18 and they were married in Limoges, France, Nov. 24, 1918. From this union there were two sons, John Albert, Jr., and Frank L., and he was inordinately proud of both. The former was lost in the Pacific in World War II when the big plane he was piloting failed to return from a bombing mission. For many months afterward Albert and his wife persisted in their hope that he might still return, and the final realization of his loss, after the end of the war, was a bitter blow. Frank married and Albert experienced the pleasure of being presented with a grandson, John Albert Key, III, shortly before his death. Mrs. Key survives and is residing in St. Louis.

Seeking to establish a permanent memorial, Albert's friends and patients have established the John Albert Key Orthopaedic Research Fellowship at the Medical School at Washington University, St. Louis, and are at present engaged in raising funds to support it. No more fitting tribute can be paid him by his friends than by sending contributions to this fund.

I know of no one of whom it can be more fittingly said "He lived a life of service to others, and the world was enriched by his existence."

—Philip D. Wilson

# Book Reviews

**Klinische Elektrokardiographie.** By Max Holzmann. Ed. 3. Pp. 687, 303 Figs. Stuttgart, Germany, Georg Thieme.

In the logical arrangement of the material, readable and fluent presentation, profuse illustration with excellent ECG records and schematic diagrams, this is one of the best textbooks available. With emphasis on clinical routine application, it exceeds the limits of strict electrocardiography with discussion of prognosis and therapy in various types of ECG abnormalities, but this is not done systematically. The theoretical background is rather condensed; for instance, the author frequently refers summarily to "animal experiments" without giving details or references. The bibliography is quite small, and there is no index of the authors' names, which would have been desirable because the references are given at the ends of the chapters. While these shortcomings are somewhat disappointing for the student in electrocardiography, they do not limit the usefulness of the book for the clinician, since sufficient background information is given for explanation of the normal and abnormal variations.

In four short introductory chapters (pp. 1-33), the history, technique, and anatomic and electrophysiologic bases are given, followed by discussion of the normal ECG (Chapter V, pp. 34-159), which includes also vectorcardiography, presented mainly as graphical reconstruction of spatial vectors from convention leads. Very few examples of oscilloscopically recorded loops are given. In view of the fluid state of vectorcardiography, such limitation is not unwise. The abnormal ECG is discussed in Chapters VI (abnormalities except arrhythmias, pp. 160-465) and Chapter VII (arrhythmias, pp. 466-638). Chapters VIII to XIII (pp. 639-677) are quite short, and are concerned with the Wolff-Parkinson-White syndrome, trauma, congenital heart disease, heart tumors, heart in neuromuscular diseases, and the dying heart.

American readers will find some interpretations and judgments which are not commonly accepted in this country. For example, septal involvement in myocardial infarctions is not diagnosed as often as it is by American electrocardiographers. On the other hand, anterior wall infarct is diagnosed from transient T wave changes in precordial leads even when the QRS complex is normal. The opinion of the author that pulmonary embolus produces a typical pattern is not supported by experience in this country which has shown that the pattern described by McGinn and White is actually found in only a minority of patients.

The author has enlarged the chapter on ECG in congenital heart disease but, in spite of this, the chapter is only 7 pages long and without illustrations. This reviewer was disappointed not to find a systematic discussion of the value of preoperative ECG for an estimate of the risk in surgery or of the usefulness of the ECG during and after cardiac surgery.

—Ernst Simonson.

**Die Grundlagen der Transplantation Von Fremdem Knochengewebe.** By Dr. Med. Wolfgang Lentz. Pp. 111. Stuttgart, Germany, Georg Thieme.

This is a very excellent short monograph on bone grafting as carried out at the University of Kiel. The author has used the technique of Maatz, which was recently described in the American literature, to evaluate the osteogenic properties of various kinds of bone grafts. There is a clear and adequate presentation of experiments in animals and experience in the treatment of a variety of conditions in patients. There is a very good analysis of the various methods of preserving bone and their effect upon the success of preserved bone grafts. Anyone interested in the subject of bone grafting should peruse this little volume with interest.

—Leonard F. Peltier.

## *Contents—(Continued from front cover)*


Total Cardiac By-pass in Humans Utilizing a Pump and Heterologous Lung Oxygenator (Dog Lungs). Gilbert S. Campbell, M.D., Norman W. Crisp, M.D., and E. B. Brown, Jr., Ph.D., Minneapolis, Minn. ---- 364

Cancer of the Breast in Indian Women. J. C. Paymaster, F.R.C.S.(Edin.), Bombay, India ---- 372

Carcinoma of the Tongue. Frank C. Marchetta, M.D., and Walter L. Mattick, M.D., Buffalo, N. Y. ---- 378

The Management of Acute Massive Venous Occlusion. John A. Rasmussen, M.D., Stanley E. Potter, M.D., and R. Russell Best, M.D., Omaha, Neb. ---- 387

A New Suture Method for Liver Resection. John R. Robinson, M.D., and Harvey R. Butcher, Jr., M.D., St. Louis, Mo. ---- 391

A New Clamp and Clamp Technique for Full-Thickness Myocardial Resection. Salem Fathi Sayegh, M.D., Baghdad, Iraq, and H. Reichard Kahle, M.D., New Orleans, La. ---- 397


### Case Reports


Peritoneal Cavity With Two Compartments. Harold F. Hamit, Lieutenant Colonel (MC) USA, and Clinton S. Lyter, Colonel (MC) USA, Denver, Colo. ---- 402

Gastrocolic Fistula Resulting From Benign Gastric Ulcer. Jessie Gray, M.D., Toronto, Canada ---- 408

Pancreatitis Occurring in Heterotopic Pancreatic Tissue. William P. Longmire, Jr., M.D., and Manfred A. Wallner, M.D., Los Angeles, Calif. ---- 412

Osteogenic Sarcoma. Bernard G. Herman, M.D., and Samuel L. Perzik, M.D., Beverly Hills, Calif. ---- 419

The Use of Polyethylene Tubing to Restore Continuity in Small Arteries. John H. Kehne, M.D., Memphis, Tenn. ---- 424


### Recent Advances in Surgery


Arterial Thrombosis Associated With Cervical Ribs: Surgical Considerations. Clarence J. Schein, M.D., Henry Haimovici, M.D., and Henry Young, M.D., New York, N. Y. ---- 428


### Editorial


Palliative Therapy in Cancer. Alton Ochsner ---- 444

Our Medical Literature Problem. Maurice B. Visscher ---- 445


### Appraisal of Progress in Surgical Therapy


A Consideration of Certain Benign Lesions of the Esophagus. Richard H. Sweet, M.D., Boston, Mass. ---- 447


### In Memoriam


John Albert Key, 1890-1955. By Philip D. Wilson ---- 459


### Book Reviews


Book Reviews ---- 464



(For Calendar of Surgical Meetings, see page 458)

(Editorial and Business Communications on page 9)

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